18th Annual Meeting, American College of Chest Physicians
Congress Hotel, Chicago, Illinois, June 5 - 8, 1952

VOLUME XXI NUMBER 1

DISEASES

of the

CHEST

OFFICIAL PUBLICATION

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1952

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XII Congress, International Union Against Tuberculosis
II International Congress on Diseases of the Chest
Rio de Janeiro, Brazil, August 24-30, 1952

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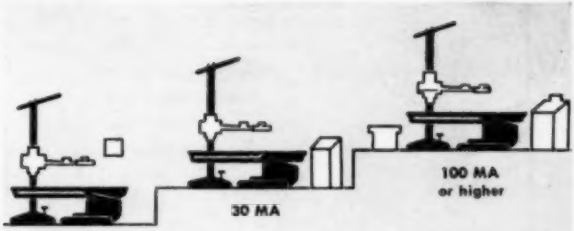

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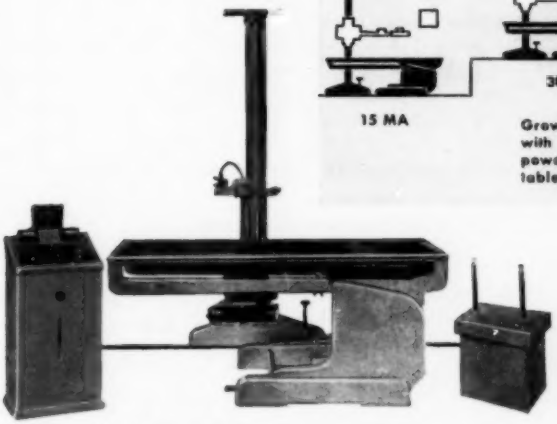

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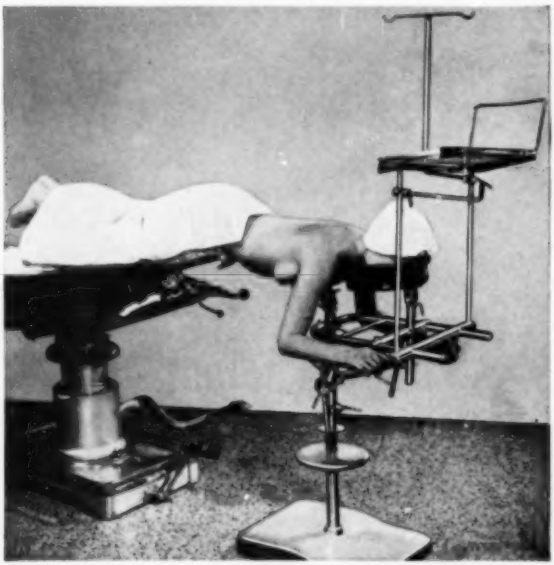

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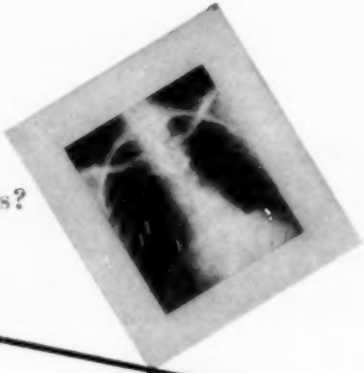

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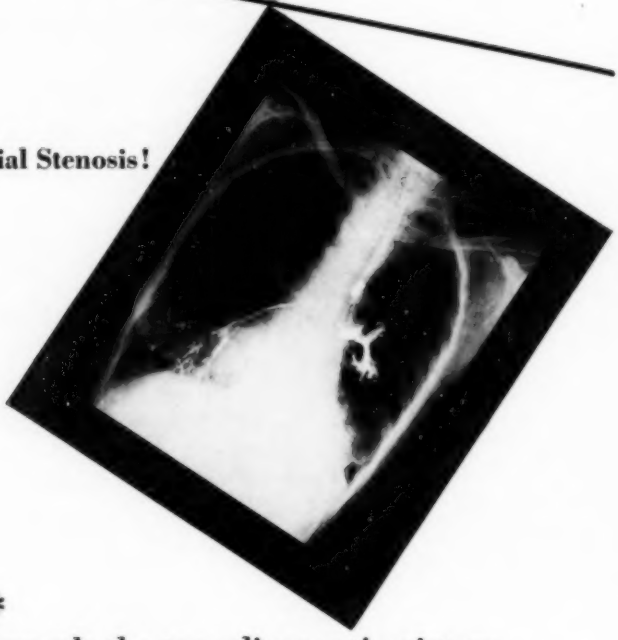

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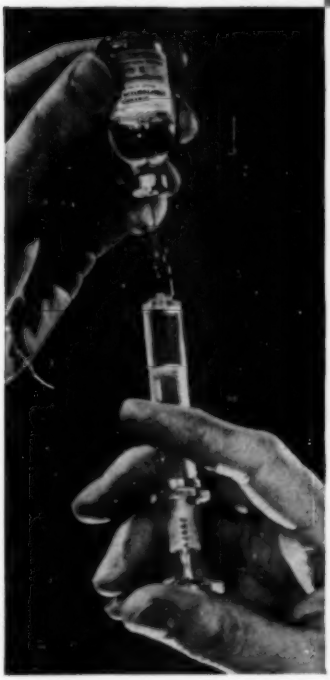

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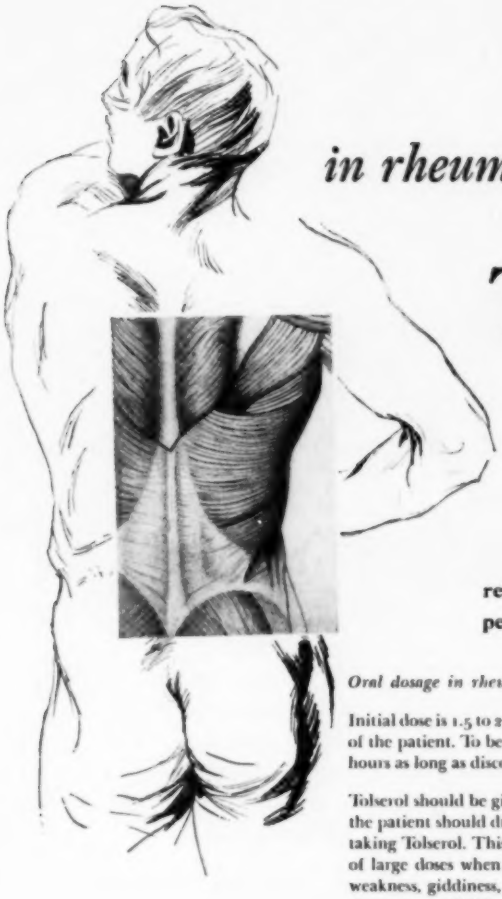

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1. J.A.M.A. 147:730-737 (Oct. 20) 1951. Literature and detailed dosage information on request.

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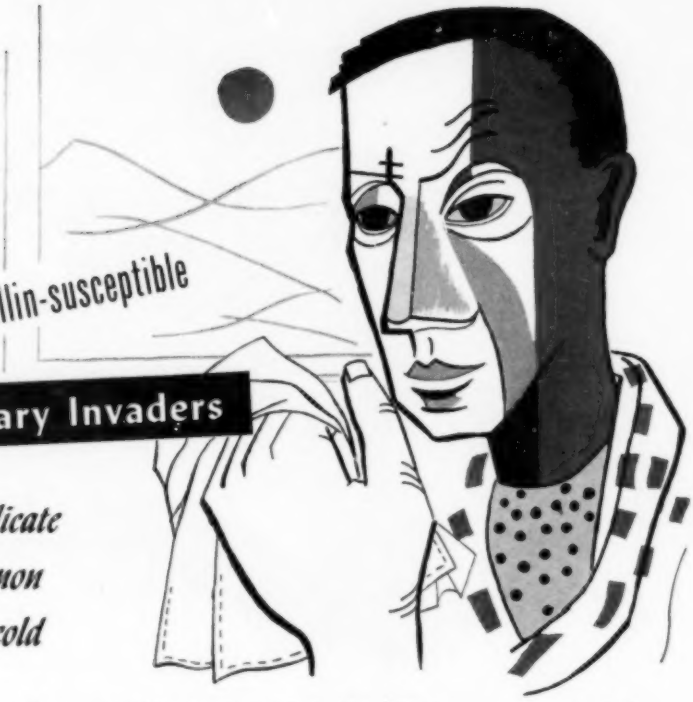

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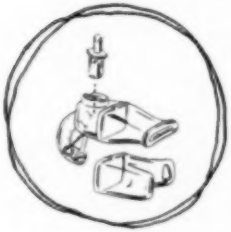

1. Krasno, L., and Rhoads, P. (1949), The Inhalation of Penicillin Dust, Amer. Prac., 11:649, July.

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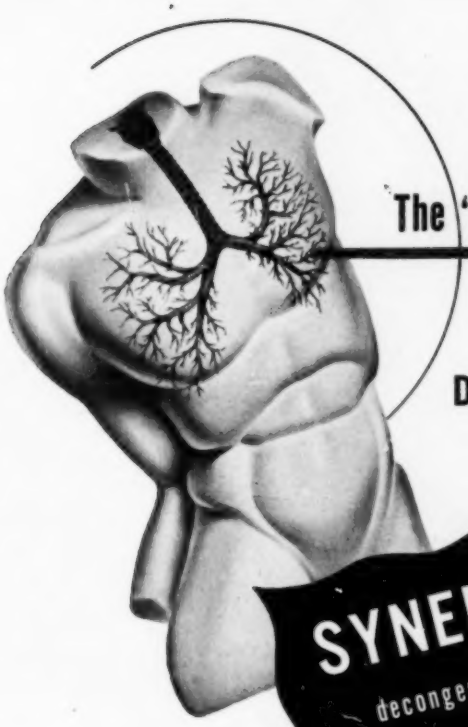

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1. Reiser, H. G., et al.: Arch. Surg. 63: 568-575 (Oct.) 1951.

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DISEASES *of the* CHEST

VOLUME XXI JANUARY 1952 NUMBER 1

Combined Intermittent Regimens in the Treatment of Non-Miliary Pulmonary Tuberculosis

A Comparison of Streptomycin Every Third Day and Para Aminosalicylic Acid Daily with Streptomycin Every Third Day and Para Aminosalicylic Acid Every Third Day*

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I. *Introduction*

In a previous report the Fitzsimons Group presented its experience with a regimen employing streptomycin (SM) 1 or 2 grams intramuscularly every third day given simultaneously with para-aminosalicylic acid (PAS) 12 grams daily by mouth for 120 days.[1,2] It was found that this combined intermittent treatment schedule was superior in most major aspects to regimens employing SM alone daily or every third day, or PAS alone daily. The suppression of bacterial resistance to both drugs when SM was given every third day with PAS daily for periods up to 120 days was especially gratifying. As the effectiveness of this regimen became apparent, study of a dosage schedule combining SM 1 or 2 grams with PAS 12 grams, each every third day, was begun on similar types of patients for a like period. Specifically it was desired to learn if the employment of PAS every third day would be as successful as PAS daily in the preservation of bacterial sensitivity to SM without reduction of clinical or roentgenographic response, since the administration of PAS every third day would meet with considerably wider patient acceptance than the daily dosage schedule.

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Investigation of a regimen employing SM and PAS each every third day was started in November 1949. One hundred and three patients who completed 120 days of therapy on this combined intermittent regimen were studied and of these 54 were followed for at least six months from the date of completion of therapy. (The reduction in number at the follow-up period is due to transfers to other hospitals and to irregular discharges.) In this paper is presented an evaluation of this combined intermittent regimen employing both drugs every third day with the previous regimen employing streptomycin every third day with PAS daily. The regimen employing SM every third day with PAS daily will subsequently be referred to as SM Q3 PAS Daily and that employing both drugs every third day will subsequently be referred to as SM Q3 PAS Q3.

II. *Methods of Evaluation*

As in the earlier study,[2] evaluations and comparisons have been made on the bases of clinical, roentgenographic and bacteriologic responses and drug toxicity.

Patients were classified as "symptomatic" or "asymptomatic" for the clinical evaluation. Symptomatic includes those who were either febrile, had weight loss in excess of five pounds below normal or loss in excess of five pounds during treatment, or who produced sputum in excess of five cubic centimeters.

Roentgenograms of the chest were evaluated by three physicians in terms of trend of the pulmonary lesion and presence of cavity. Trend was graded as improved, unchanged or worsened. Worsening was recognized if any degree of extension of the disease occurred in any part of the roentgenogram even if other areas were improved. Presence of cavity was recorded only if the outline could be clearly seen.

Bacteriologic evaluation of sputum was made by accepted smear and culture techniques and of fasting gastric contents by culture alone.[3] Sputum was defined as "converted" if negative by culture for three consecutive months. Patients whose sputum or gastric studies were negative for a period of less than three months at the evaluation date were called "indeterminate".

Sensitivity studies to both drugs were performed on Herrold's egg yolk agar at approximately bi-monthly intervals during therapy, and monthly thereafter.[4] After 10 to 14 days of incubation growth on media containing the drug was evaluated by comparison with the control. Cultures showing growth on the 10 mcg./ml. tube equal to that on the control (0 mcg./ml.) were called "resistant".[5]

Evaluation of clinical, roentgenographic and bacteriologic data

was made at the following periods: (a) At the date of onset of drug treatment for the 60 days immediately preceding therapy to establish the trend at the zero day, (b) at the completion of therapy (120 days) in relation to the zero point, and (c) at six months from the 120 day point.

III. *Analysis of Clinical Material*

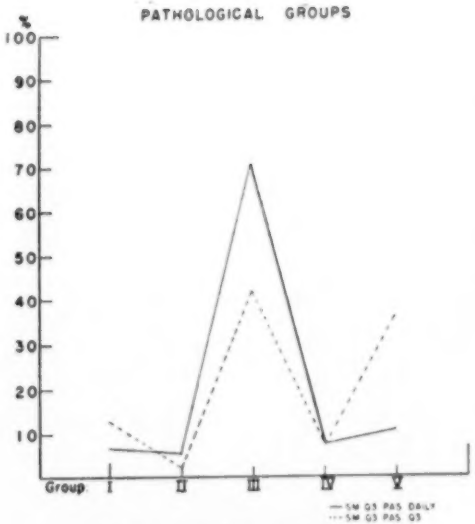
The following requirements of the study were identical for the two regimens: (a) Moderately or far advanced non-miliary pulmonary tuberculosis with tubercle bacilli sensitive to both drugs demonstrated at beginning of therapy, (b) no previous SM, PAS or other tuberculostatic drug treatment, (c) deferment of operative procedures until completion of at least 120 days of drug therapy, and (d) maintenance of uniform standards of rest treatment.

A comparison at the zero day of the case material studied on the two regimens is presented in Table I.

In general, the types of patients treated are fairly similar, consisting of otherwise healthy young white males with disease of predominantly recent origin. A significant difference between the two series at onset of drug therapy is a higher incidence of far advanced and of cavitary disease in the first regimen (SM Q 3 PAS Daily). On the other hand, there is a significantly lower incidence of roentgenographically progressive disease, and proportionately higher incidence of stationary disease at the zero day point in that regimen. Complications included endobronchial and laryngeal tuberculosis, hemoptysis, pleural effusion, gastrointestinal and other types of extrapulmonary tuberculosis. These were recorded when they existed or appeared at any time during the course of treatment or during the follow-up period. No instances of miliary tuberculosis or meningitis were encountered. The incidence of non-tuberculous complicating diseases was negligible.

Each case was assigned a clinical pathological classification based primarily upon comparison of serial roentgenograms with consideration of clinical course.[6] As shown graphically (Figure 1), the pattern of distribution is generally similar for the two series, with a significantly lower proportion of new mixed lesions (exudative and caseous pneumonic, type III) and higher proportion of mixed new and old lesions (type V) in the group treated with both drugs every third day.

The evaluation at six months from the end of chemotherapy is made primarily to reflect the overall status of those patients followed for that length of time rather than the effect of the drug treatment alone. As shown in Figure 2, the great majority



CLINICAL PATHOLOGICAL CLASSIFICATION

I NEW, RESOLVING LESIONS (Exudative)
II NEW, POORLY RESOLVING LESIONS (Caseous Pneumonic)
III NEW MIXED LESIONS (Exudative, Caseous Pneumonic)
IV OLD, IRREVERSIBLE LESIONS (Fibro-Caseous)
V MIXED NEW AND OLD LESIONS

FIGURE 1 PERCENTAGE DISTRIBUTION OF CASES BY CLINICAL PATHOLOGICAL TYPES

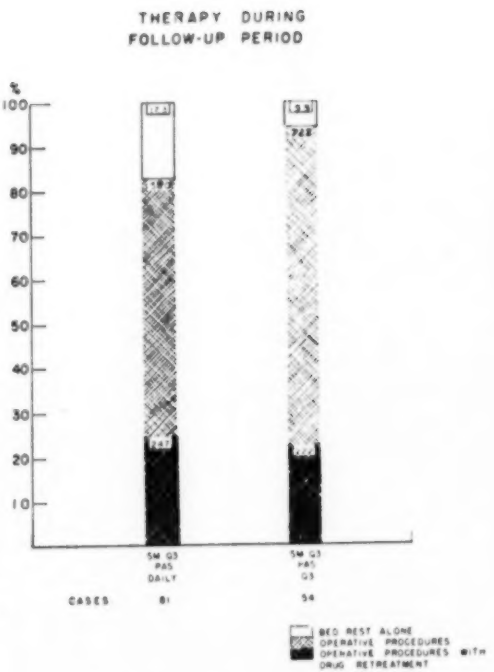


FIGURE 2 PERCENTAGE OF CASES RECEIVING VARIOUS TYPES OF THERAPY DURING FOLLOW-UP PERIOD

in both series (82.7 per cent of the 81 patients followed for six months after completion of SM Q 3 PAS Daily and 94.4 per cent of the 54 patients followed for six months after completion of SM Q 3 PAS Q 3) subsequently underwent operative procedures (temporary or permanent collapse or resection), in many instances with drug re-treatment. It is noteworthy that only 5 to 20 per cent of the patients on either regimen needed no further treatment other than bed rest. It is also interesting that no patient received drug re-treatment alone during the follow-up period. In all instances where drug re-treatment was prescribed, some form of collapse or surgical procedure was also indicated.

IV. *Evaluation After 120 Days of Drug Treatment and Six Months Subsequently*

Clinical Status: In Figure 3 is shown the clinical status of patients studied on the two regimens at the start of therapy (zero day), at completion of 120 days of therapy and six months from the latter date. To facilitate comparison the number of patients evaluated on each regimen at each time period is considered 100

TABLE I
PRETREATMENT STATUS

	SM Q 3 PAS DAILY		SM Q 3 PAS Q 3	
	Number	Per cent	Number	Per cent
Historical:				
Total Number Cases	95	100.0	103	100.0
Average Age (years)	29.4	—	26.9	—
Race (White)	80	84.2	92	89.3
Sex (Male)	88	92.6	100	97.1
Clinical:				
Duration (months), Under 6	61	64.2	44	42.7
7 to 18	21	22.1	32	31.0
Over 18	13	13.7	27	26.2
Symptomatic	84	88.4	83	80.6
Asymptomatic	11	11.5	20	19.4
Complications (Tuberc.)	19	20.0	16	15.5
Roentgenographic:				
Extent of Disease, Moderately Advanced	53	55.8	74	71.8
Far Advanced	42	44.2	29	28.2
Trend:				
Regressive	17	17.9	18	17.5
Stationary	64	67.4	61	59.2
Progressive	14	14.7	24	23.3
Cavitary	83	87.5	61	59.2

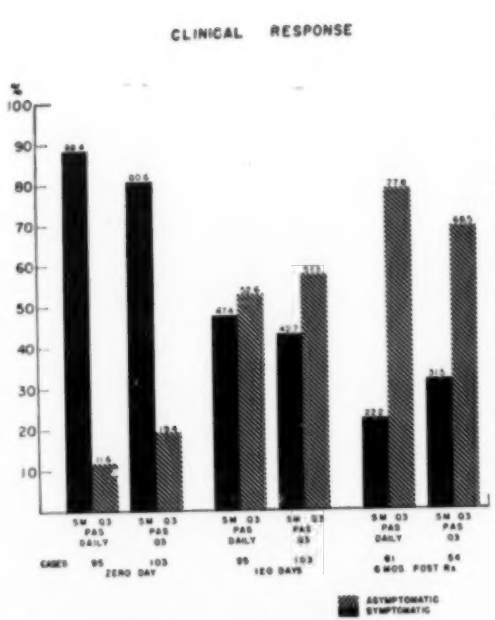


FIGURE 3. PERCENTAGE OF CASES SYMPTOMATIC AND ASYMPTOMATIC ON EACH REGIMEN AT START AND COMPLETION OF DRUG THERAPY, AND SIX MONTHS SUBSEQUENTLY.

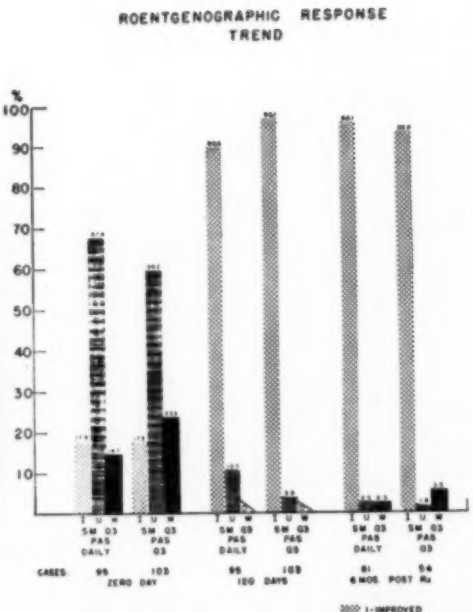


FIGURE 4. ROENTGENOGRAPHIC EVALUATION, PRE-TREATMENT TREND(ZERO DAY), RESPONSE DURING AND AFTER DRUG TREATMENT IN COMPARISON TO STATUS AT ZERO DAY.

per cent. According to the criteria previously stated the great majority of patients on both regimens were symptomatic at the zero day. After 120 days of combined intermittent therapy approximately an equal proportion of the patients on each regimen were symptomatic and asymptomatic. Evaluation six months from completion of chemotherapy reveals that the proportion of asymptomatic patients has approximately doubled in comparison to those still symptomatic. This, of course, is largely the result of further treatment received subsequent to the initial course of chemotherapy (see Figure 2).

Roentgenographic Evaluation: In Figure 4 is shown the roentgenographic response in terms of percentage improved, unchanged and worsened. These values at the zero day point refer to trend during the 60 days prior to chemotherapy. Trend is evaluated at the 120 day point in comparison to status at the zero day point. In both regimens a marked change is noted in the pattern at 120 days with approximately 90 per cent showing roentgenographic improvement, 10 per cent or less unchanged, and no instances of worsening. Trend at 120 days shows a slight advantage in favor of the SM Q 3 PAS Q 3 regimen (larger percentage improved, smaller percentage unchanged). Roentgenographic trend at six months from completion of chemotherapy in comparison to the zero day is also shown in the same figure. It is noted that on both regimens the striking improvement apparent at 120 days is maintained. A very small and approximately equivalent proportion of patients on each regimen is unchanged or worsened at six months from completion of therapy in comparison to status at start of therapy. In this connection it will be recalled (Figure 2) that the majority of the patients received collapse or surgical procedures and in some instances chemotherapy during the six months follow-up period.

In Figure 5 is shown the percentage of patients studied on each regimen with cavity in the roentgenogram at zero day, at completion of 120 days of drug treatment, and at six months from the latter date. There is a considerable difference in the incidence of cavity at the zero day, 87.5 per cent of the 95 patients treated on the SM Q 3 PAS Daily regimen showing cavity in comparison to only 59.2 per cent of the 103 patients on the SM Q 3 PAS Q 3 regimen. This disparity is maintained at 120 days and at six months subsequently. At completion of the course of chemotherapy the incidence of cavity had fallen to 69.5 and 43.7 per cent respectively on the two regimens. Six months following completion of chemotherapy, during which time the majority of the patients received temporary or permanent collapse procedures and some received additional chemotherapy as well, the percentage of pa-

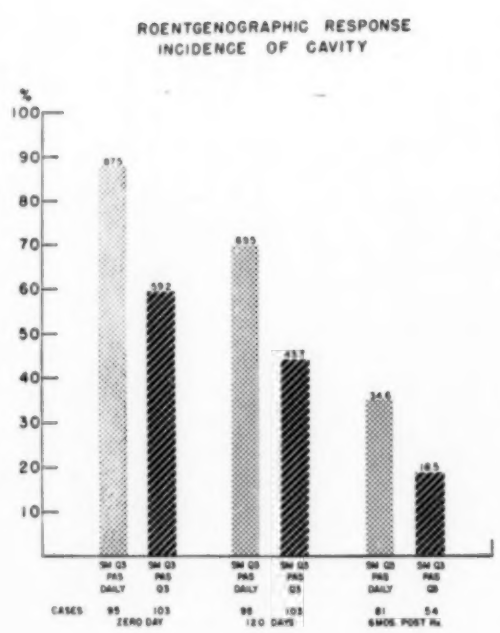


FIGURE 5. PERCENTAGE OF CASES ON EACH REGIMEN WITH CAVITY PRESENT AT ONSET AND COMPLETION OF DRUG THERAPY, AND SIX MONTHS SUBSEQUENTLY.

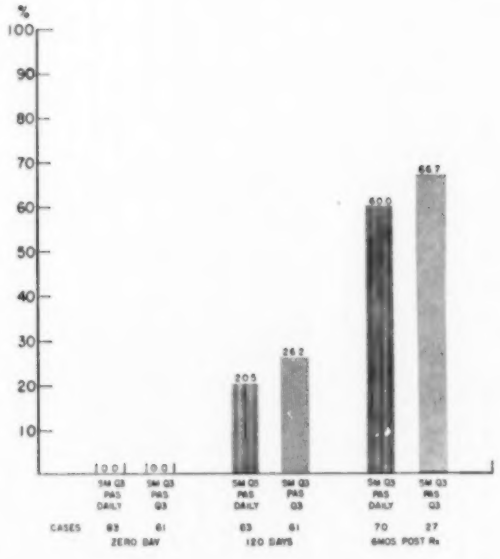


FIGURE 6. PERCENTAGE OF CASES ON EACH REGIMEN WITH CAVITY AT ZERO DAY WHICH HAD APPARENT CAVITY CLOSURE DURING AND SIX MONTHS AFTER CHEMOTHERAPY.

tients followed for that period with cavity is 34.6 and 18.5 per cent on the SM Q 3 PAS Daily and the SM Q 3 PAS Q 3 regimens, respectively. One additional patient on the latter treatment schedule had no cavity at zero or 120 days but had developed cavity at the six months follow-up period.

The incidence of apparent cavity closure at 120 days and at six months post treatment is expressed as a percentage of the number of patients with cavity at zero day (see Figure 6). After 120 days of therapy, apparent closure had occurred in 20.5 per cent (SM Q 3 PAS Daily) and 27.0 per cent (SM Q 3 PAS Q 3) of the patients with cavity at zero day on the two regimens. In other words, when cavities existed at the onset they were lost to view in only one-fifth to one-fourth of the patients during drug treatment. The same ratio of apparent closure is maintained between the two regimens at the six months evaluation point, where the percentage of cavity lost to view becomes 60.0 and 66.7 per cent, reflecting primarily response to operative procedures during that period. The slightly higher percentage of closure with the SM Q 3 PAS Q 3 dosage schedule is probably related to the lower incidence of far advanced disease in that group (39.3 as compared to 50.6 per cent) rather than to any particular attribute of the regimen itself.

Bacteriologic Status: Sputum Conversion (Figure 7): At the onset of chemotherapy 100 per cent of the patients studied on each regimen yielded cultures positive for tubercle bacilli. After 120 days of chemotherapy the incidence of patients whose sputa had converted to negative was 36.8 per cent on the SM Q 3 PAS Daily regimen and 50.5 per cent on the SM Q 3 PAS Q 3 regimen. The incidence of patients whose sputa became indeterminate (negative, but for less than three months) was 29.5 and 19.4 per cent, respectively, on the two regimens, giving a total of 66.3 and 69.9 per cent of the patients whose sputa were negative after 120 days of therapy. Six months later the percentage of patients followed for that time remaining persistently positive had changed relatively little: 34.6 per cent of the 81 patients treated with SM and daily PAS and 24.1 per cent of the 54 patients treated with both drugs intermittently. In noting the favorable trend toward negativity reflected by the status six months from completion of therapy on either dosage schedule, it should be recalled that the majority of these patients received other treatment during their follow-up period. Approximately the same proportion of sputum negativity was achieved using either regimen.

Incidence of Resistant Organisms (Table II): At the onset of chemotherapy 100 per cent of the patients studied on both regimens yielded cultures sensitive *in vitro* to 10 micrograms per milliliter concentration of SM and of PAS. After 120 days of chemo-

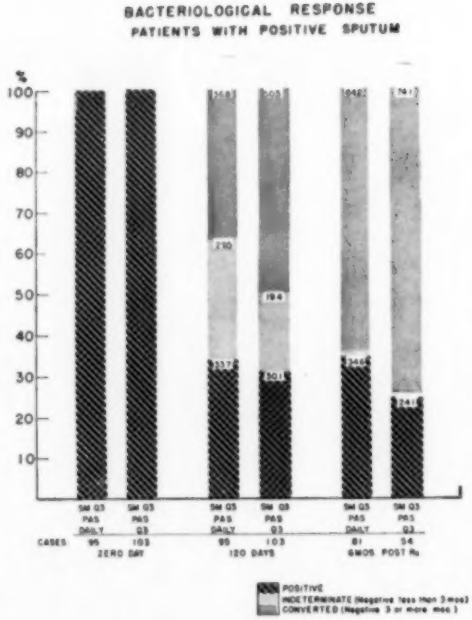
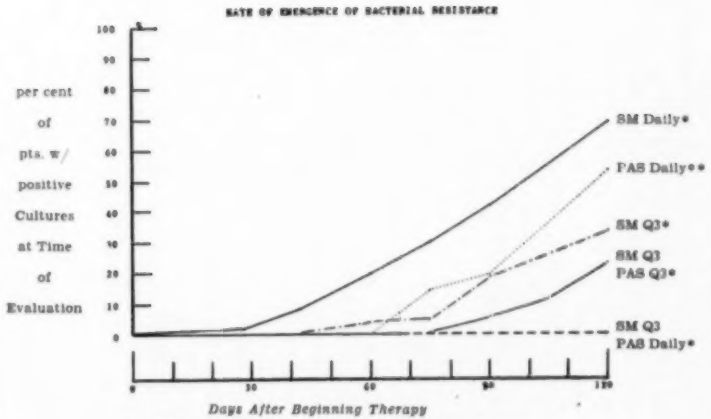


FIGURE 7. RESULTS OF SPUTUM CULTURES (PERCENT) BY REGIMENS AT ONSET AND COMPLETION OF CHEMOTHERAPY, AND AT SIX MONTHS SUBSEQUENTLY.



*per cent resistant to SM only (No PAS resistance was encountered in cases treated on combined regimen).

**per cent resistant to PAS only.

FIGURE 8. RATE OF EMERGENCE OF TUBERCLE BACILLI RESISTANT TO 10 MICROGRAMS OF CHEMOTHERAPY AGENT PER MILLILITER OF CULTURE MEDIUM DURING 120 DAYS OF THERAPY.

therapy all of the patients treated with SM every third day and PAS daily from whom positive cultures were obtained were still sensitive to both drugs. On the other hand, of the 31 patients treated with both drugs every third day from whom positive cultures were obtained at the 120 day evaluation point, cultures from nine, or 29.0 per cent, were resistant to SM, one, or 3.2 per cent, is positive with unknown sensitivity,* and cultures from the remaining positive cases were sensitive to both drugs. The incidence of bacterial resistance to SM encountered on the SM Q 3, PAS Q 3 regimen is therefore 29.0 per cent of the patients with positive cultures at completion of 120 days of therapy, but only 8.7 per cent of the 103 patients treated on that regimen for 120 days. In every instance in our experience to date when tubercle bacilli are recovered from patients whose sputums have become positive after 60 or more days of negativity, the organisms have invariably been sensitive to both drugs. Therefore it is felt that the true incidence of bacterial resistance may also be expressed in proportion to the total number of patients treated as well as in proportion to the number remaining positive at the end of treatment.

It is interesting that three of the nine patients whose organisms developed resistance to SM when treated for 120 days on SM Q 3 PAS Q 3 regimen yielded sensitive tubercle bacilli at approximately the second month following cessation of treatment, so that the "net resistance" is six of 31 or 19.3 per cent of the positive cases, or 5.8 per cent of the total number. This phenomenon of "loss of

*A single positive culture obtained after 90 days of negativity was contaminated during the course of sensitivity determination.

TABLE II

BACTERIOLOGIC RESPONSE
INCIDENCE OF RESISTANT ORGANISMS*

	— — 120 DAYS — —		6 MONTHS POST RX	
	SM Q 3 PAS Daily	SM Q 3 PAS Q 3	SM Q 3 PAS Daily	SM Q 3 PAS Q 3
Number of Cases Studied	95	103	81	54
Positive	32	31	28	13
Resistant*	0	9	1	6
Unknown sensitivity	0	1	0	0
Pct. Resistant* of Positive Cases	0.0	29.0	3.6	46.2
Pct. Resistant* of Total Cases	0.0	8.7	1.2	11.1

*Growth on media containing 10 mcg. SM per ml., comparable to growth on control (0 mcg./ml.). No resistance to PAS encountered.

bacterial resistance" has previously been encountered in four of 22 patients resistant after treatment with SM alone every third day, and in five of six patients resistant after treatment with PAS alone daily for 120 days.[2] In each of these instances therapy had been terminated at about the time of first appearance of bacterial resistance which was of slight degree. These observations suggest that the persistence of bacterial resistance is directly related to the duration of chemotherapy after resistant organisms first appear and to the degree of resistance encountered.

Of 20 patients treated for 120 days with SM every third day and PAS daily and who subsequently received further chemotherapy of from two to four months duration, positive cultures were obtained at the six month evaluation point in only nine instances. In eight of these, the organisms were sensitive to both drugs. Cultures from one patient became resistant to SM after the eighth month of continuous chemotherapy. This patient, a 22 year old white female with far advanced, bilateral, fibrocavitary tuberculosis and progressive downhill course, had received SM every three days and PAS daily for eight consecutive months with unfavorable clinical and roentgenographic response.

Thirteen of the 54 patients treated with both drugs every third day and followed for six months yielded positive cultures at that time. Of these, six or 46.2 per cent were resistant to SM. Four had maintained resistance from the 120 day point, and two developed resistance coincident with additional chemotherapy during the follow-up period. Cultures from the remaining seven patients were sensitive to both drugs six months post treatment.

The average length of time for SM resistance to develop has been shown to vary considerably with different treatment regimens.[7] When SM alone was given daily in doses of 1 or 2 gms., the average time for development of resistance was 67 days. When SM was given alone every third day, resistance developed in 89 days. When SM was given every third day with PAS also every third day the average length of time for development of SM resistance was 106 days. Thus, from the standpoint of delaying as well as suppressing the appearance of resistant organisms, SM every third day with PAS every third day is superior to SM alone, either daily or every third day.

Comparison of the nine patients who yielded tubercle bacilli resistant to SM after 120 days of therapy with both drugs intermittently to the 21 patients with cultures positive and sensitive after 120 days of therapy, reveals no significant differences in the extent of disease, incidence of cavity, pathological type of disease, clinical and roentgenographic response, or incidence of tuberculous complications. This is not surprising when one con-

siders that these nine patients received an average of 106 days of chemotherapy before resistance to SM appeared.

The only differences between the combined intermittent regimens compared in this paper are the quantity and time of administration of PAS. Emergence of bacterial resistance to SM on the regimen employing PAS intermittently (SM Q 3, PAS Q 3) but not on the daily PAS regimen (SM Q 3, PAS daily) suggests that it is necessary to give a certain minimal quantity of PAS in order to obtain an adequate "combined therapy" effect.[8] This concept is substantiated by experiences with the PAS salt of SM[9,10] and with varying doses of PAS in combination with daily SM.[11]

Rate of development of bacterial resistance (Figure 8) is best shown by reference to larger series of patients in whom this phenomenon has been studied.[5] The two treatment schedules reported in this paper may be compared to our experience with earlier regimens studied by the same techniques in the same laboratory.[2] Resistance to SM appears earliest and reaches highest incidence when the drug is administered daily. The appearance of resistant organisms is delayed, and the incidence reduced by more than 50 per cent when streptomycin is given intermittently every third day. Administration of PAS alone in daily dosage results in the appearance of resistant organisms in 53.1 per cent of those patients remaining positive after 120 days of therapy. When the two last mentioned regimens are combined, namely, SM every third day simultaneously with PAS daily no organisms resistant to 10 mcg./ml. of either drug are encountered. On the other hand, when both drugs are given every third day a small percentage of the patients remaining positive yield organisms resistant to SM only. From the standpoint of delaying bacterial resistance, then, SM every third day with PAS daily is the preferred regimen, but SM every third day with PAS also every third day is superior to either drug alone, daily or (in the case of SM) intermittently, for periods up to 120 days.

Toxicity: Incidence of drug toxicity encountered during 120 days of treatment with SM every third day and PAS daily was 13.1 per cent and sufficient to cause cessation of therapy in four of these cases, or 4.2 per cent.[2] Only one patient (1.0 per cent) of the 103 treated with both drugs every third day was found to have clinical evidence of toxicity during 120 days of therapy. This patient had mild dermatitis which cleared completely following cessation of drug therapy. No instances of toxicity sufficient to require interruption of therapy were encountered in the series treated with both drugs intermittently. The incidence of gastrointestinal distress from the latter regimen was clinically insignificant in contrast to previous experience with daily PAS re-

gimens. From the standpoint of patient acceptance, the combined intermittent regimen employing PAS every third day possesses an advantage over that employing daily PAS.

V. SUMMARY

1) A comparison of two groups of patients with proved pulmonary tuberculosis of moderate and far advanced extent has been presented. One series of 95 patients was treated with streptomycin every third day and para aminosalicylic acid daily for 120 days; the other series of 103 patients received streptomycin every third day and para aminosalicylic acid every third day for 120 days. Six months follow-up study has been completed on 81 and 54 patients respectively.

2) Both groups were compared in regard to age, sex, race, extent of disease, pathological type, roentgenographic and clinical status at the start of therapy.

3) Results of treatment evaluated at the 120 day point and at six months post treatment were as follows:

(a) Clinical response was approximately equivalent for the two regimens at 120 days. Further improvement occurred during the follow-up period in both groups, but to slightly greater extent in those treated with streptomycin every third day and para aminosalicylic acid daily.

(b) Marked roentgenographic improvement was observed during 120 days of therapy and at six months post treatment with both regimens. No worsening occurred during the 120 days of therapy. Only 20.5 to 26.2 per cent of cavitary cases had apparent cavity closure during treatment, but 60.0 to 66.7 per cent had cavity closures during the six month follow-up period, due largely to addition of operative procedures.

(c) On the two regimens 66.3 to 69.9 per cent of the patients had negative sputa after 120 days. The proportion remained approximately the same at the six month evaluation.

(d) None of the patients treated with streptomycin every third day and para aminosalicylic acid daily for 120 days yielded tubercle bacilli resistant to either drug. Of the patients treated with both drugs every third day nine or 29.0 per cent of those with positive cultures, or 8.7 per cent of the total yielded organisms resistant to streptomycin after 120 days of treatment. Bacterial resistance did not appear in these nine patients until they had received an average of 106 days of drug therapy. Comparison of the patients whose sputa yielded resistant organisms to those whose sputa yielded sensitive organisms after treatment revealed no material difference. A phenomenon of "loss of bacterial resistance" to

streptomycin was encountered, and its significance discussed briefly. Bacterial resistance to para aminosalicylic acid did not occur. Comparison of the incidence of bacterial resistance to streptomycin encountered in the series treated with both drugs every third day in comparison to earlier studies performed according to the same methods in the same laboratory revealed a lower incidence of sensitivity when both drugs are administered every third day than when either is administered alone daily, or in the case of streptomycin, every third day.

(e) Drug toxicity was not a major problem in either regimen. Significantly less gastro-intestinal disturbance was encountered when para aminosalicylic acid was administered every third day.

CONCLUSIONS

Combined intermittent therapy employing streptomycin every third day and para aminosalicylic acid daily is, in our experience, the regimen of choice when specific drug therapy is indicated for the treatment of non-miliary pulmonary tuberculosis for periods up to four months. A second form of combined intermittent therapy employing both drugs every third day is equally effective clinically, roentgenographically and in terms of sputum conversion, but possesses the disadvantage that bacterial resistance to streptomycin is encountered in a small percentage of cases. This second regimen, however, may be used to advantage in patients who are unable to take para aminosalicylic acid daily for long periods and is superior to the use of either streptomycin or para aminosalicylic acid alone for 120 days.

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RESUMEN

Según nuestra experiencia el régimen de estreptomicina cada tercer día y ácido paraminosalicílico a diario es el de elección cuando este tratamiento está indicado para las formas no miliares de tuberculosis pulmonar durante periodos hasta de cuatro meses. Otra forma de emplear estas drogas es usándolas ambas cada tercer día y es efectiva tanto clínica como roentgenológicamente así como en lo que respecta a la conversión de esputos pero tiene la desventaja de que la resistencia bacteriana a la estreptomicina se encuentra en un porcentaje pequeño de casos. Sin embargo el segundo régimen puede emplearse en los enfermos que no queden usar el PAS a diario por largos periodos de tiempo y es superior al uso de la estreptomicina o el PAS aisladamente, por 120 días.

RESUME

Le traitement combiné utilisant la streptomycine tous les trois jours et le P.A.S. quotidiennement est, pour les auteurs, le procédé de choix quand le traitement spécifique est indiqué pour une durée supérieure à quatre mois dans la tuberculose nonmiliaire. Ils ont utilisé également un autre mode d'administration de ces deux drogues: il consiste à les utiliser toutes les deux ensemble, tous les trois jours. Les résultats sont assez favorables, cliniquement, radiologiquement et bactériologiquement mais il a l'inconvénient de permettre dans un petit nombre de cas l'apparition d'une résistance à la streptomycine. Cette seconde technique a cependant des avantages dans les cas de malades qui ne peuvent pas prendre pendant longtemps du P.A.S. chaque jour, et il est supérieur à l'utilisation de la streptomycine ou du P.A.S. à titre isolé pendant cent vingt jours.

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Empyema Complicating Closed Intrapleural Pneumonolysis and Artificial Pneumothorax*

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Despite many viscissitudes, pneumothorax is still the most important collapse measure in pulmonary tuberculosis. Its accessory procedure, closed intrapleural pneumonolysis, has increased greatly in usefulness and popularity and is considered to have very few complications. The most important one is tuberculous empyema which, in various published series[1-10] ranges from zero to 26 per cent with a median range of 4 to 8 per cent. The great majority of these figures is based upon postoperative observation of from one to four months. The occurrence of empyema beyond this time is assumed to be due to nonoperative causes.

According to Alexander,[2] some surgeons "do not consider even a pleuro-pulmonary perforation with a mixed infection empyema as a postoperative complication if it occurs more than a month or two after operation." He also states that "the incidence of serious postoperative complications is almost in direct ratio to the shortness of the adhesion divided and in inverse ratio to the experience, skill, and patience of the surgeon."

In this study it will be shown: (1) that other factors contributing to empyema formation include several features of the adhesions and certain parenchymal characteristics, (2) that the empyema rate varies directly with the difficulty of the operation, (3) that the empyema rate is higher than generally supposed, and (4) that from the empyema standpoint there is no definite postoperative period limited to three months but an indefinite one limited only by the duration of the pneumothorax.

Material

This study deals with a group of 151 closed intrapleural pneumonolyses done on 151 patients. In almost all of the cases there

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were so many extensive adhesions that the series was classified as a "difficult pneumonolysis group." We appreciate the difficulty in labeling a pneumonolysis as difficult or easy, since that varies so much with the expertness of the operator and the number, character, and location of the adhesions. If only the easy adhesions are severed, then the operation is an easy one but if, in addition, the short and sheet-like adhesions are severed or stripped, including those to the mediastinum, then the operation may indeed become a difficult one. In this group of cases the character, extent and location of the adhesions plus those actually severed make it a "difficult group" under all criteria. This specification is important since it is in such cases that a high empyema rate is to be expected.

This series of 151 cases was done over a nine-year period from October 1936 until December 1945, with an observation period extending another 27 months until March 1948. The average period of observation for the group was 44 months, or almost four years. The pneumonolyses were compared with a control group of 863 pneumothoraces done and observed during the same period of time; these were further subdivided into 462 effective and 401

TABLE I

Comparison of the More Important Features of the Three Groups of Cases (Nearest whole percentage)

Feature	Effective Pneumothorax 462 cases	Ineffective Pneumothorax 401 cases	Pneumonolysis 151 cases
Extent of Involved Side:			
Far advanced	58	84	85
Moderately advanced	39	16	15
Character:			
Exudative	81	83	69
Productive	13	8	22
Cavities:			
Average size (cm.)	4.5	7.0	7.0
None	9	6	2
To 4 cm.	67	36	37
4 to 8 cm.	22	44	44
8 cm.	2	14	18
Thick Cavity Wall	7	26	38
Numerous adhesions	34	73	59
Duration of pneumo, months	38	13	32
Duration of observation, months	58	26	44

ineffective collapses. An effective pneumothorax was defined as one in which the collapse resulted in cavity closure and control of the disease in the specified lung, whereas in an ineffective pneumothorax a residual cavity persisted. Any complicating empyema occurred either during the effective or the ineffective period. As used here, the term empyema means the presence of gross, frank pus. Serous and serofibrinous effusions (bacillary or otherwise) were excluded. All cases were operated upon by Dr. Edgar W. Davis with the Corylios-Unverricht-Jacobaeus thoracoscope with two cannulae and galvanocautery.

Comparability of the Three Groups of Cases:

Table I shows the more important characteristics of the disease exhibited by the effective pneumothorax group, the ineffective group, and the pneumonolysis cases.

The EFFECTIVE pneumothorax group included 462 pneumothoraces in 411 patients, 51 of whom were bilaterally collapsed. There occurred eventually 475 effective collapses but, since 13 cases developed empyema while still ineffective, they were included with the latter group. The disease was far advanced in 72 per cent of the patients and, using the bilateral classification of Salkin and Cadden,[11] the pneumothorax lungs showed far advanced disease in 58 per cent. The other features are shown in the table. Cavity closure occurred in an average time of 6.8 months; the average collapse was three years and the observation period almost five years.

The INEFFECTIVE group comprised 401 pneumothoraces in 380 patients, of whom 21 had bilateral collapse. Far advanced disease was present in 93 per cent of the patients and in 84 per cent of the collapsed lungs. The average pneumothorax period was slightly over one year and the observation period over two years. The reasons for maintaining the pneumothoraces for such a long period of time were the inability of some patients to obtain a thoracoplasty (medical or financial), the symptomatic relief obtained, and the current custom of maintaining ineffective collapses for a longer period of time. This group forms an excellent control.

The PNEUMONOLYSIS group comprised 151 operations done on 151 patients. Far advanced disease was present in 91 per cent of the patients and in 85 per cent of the individually collapsed lungs. The duration of the pneumothorax in 53 reexpanded lungs averaged 31 months; and for the whole group 32 months with an observation period of 44 months.

In comparing the three groups it is seen that the greatest number of far advanced sides occurred equally in the Ineffective pneumothoraces and in the pneumonolyses. Exudative disease predom-

inated in the two pneumothorax groups. Cavitation was equal in the Ineffective pneumothorax and pneumonolysis cases. The greatest number of adhesions occurred in the Ineffective group, a lesser number among the pneumonolyses, and the smallest number in the Effective pneumothorax cases.

Considering these features it may be concluded that the Ineffective group was the most severe and the least likely to respond therapeutically. The pneumonolysis cases were next in order of severity, and the Effective pneumothorax cases the least severe. It is further estimated that the Ineffective cases were about 50 per cent more severe than the effective cases, and that the pneumonolysis cases stood about midway between the two pneumothorax groups. This feature must be taken into account when comparing empyema rates, since it is to be expected that the more severe the disease the more likely the occurrence of empyema.

Incidence of Empyema

The effective pneumothoraces showed an incidence of 8.4 per cent empyema; the ineffective 12.9 per cent; the pneumonolyses 31.7 per cent; a ratio of 1 to 1.5 to 3.7 respectively. This incidence did not extend over the usual postoperative period of three months but over the entire period the patient was observed, which averaged 58 months for the effective group, 26 months for the ineffective group, and 44 months for the pneumonolysis group.

Analysis of the Empyemas

The EFFECTIVE control group had 39 empyemas in 462 collapses. The average pneumothorax became effective in 6.8 months. Table II presents the important factors. About two-thirds of the empyemas occurred in 12 months and 80 per cent at 18 months. There were no empyemas in 15 minimal cases, and the rate was highest in the far advanced group. The 19 cases of fibroid and nine mixed disease gave rates of 10 and 33 per cent respectively, but their numbers were too small for inclusion. The larger the size of the cavity, the thicker the cavity wall, and the greater the number of adhesions, the higher was the empyema rate.

The INEFFECTIVE group had 52 empyemas in 401 pneumothoraces. The time period of development was similar to the effective cases (Table II). In this group, the 22 cases of fibroid disease and 15 mixed disease showed 4.5 and 6.6 per cent empyema but again the numbers were too small for inclusion. The highest rates were noted in cases with far advanced disease, large cavities, and numerous adhesions. The thickness of the cavity wall showed no influence.

The PNEUMONOLYSIS group had 48 empyemas. The time period

of development was more rapid, for 91 per cent occurred within 12 months after the operation with quarterly figures of 16.6, 34, 23, and 18 per cent. As in the above groups, the highest rates occurred in far advanced cases, exudative disease, large cavities, and the presence of many adhesions. The thickness of the cavity wall appeared to be a factor; in evaluating this finding such associated features as exudative disease, numerous adhesions, and gross bronchitis appeared to have no influence, since they were equally distributed in thin, medium, and thick-walled cavities.

The two *control pneumothorax groups* combined had 91 empyemas in 863 pneumothoraces, or 10.5 per cent. The involved side was far advanced in 70 per cent of the cases, moderate in 28 per cent, and minimal in 2 per cent. Exudative disease occurred in 81 per cent and productive in 11 per cent. Cavitation was present in 92 per cent, with 52 per cent in cavities up to 4 centimeters, 32 per cent from 4 to 8 centimeters, and 8 per cent over 8 centimeters. Numerous adhesions were present in 52 per cent. Sex, age,

TABLE II

Percentage of Empyema Development Related to the More Important Factors

		Effective	Ineffective	Lysis
Time of Development Cumulative percentage of empyema group	End of 3 Mos.	18	4	16
	End of 6 Mos.	41	20	51
	End of 12 Mos.	66	66	91
	End of 18 Mos.	79	80	93
	End of 24 Mos.	82	90	95
Extent of involved side	Moderate	4	1.5	5
	Far advanced	12	15	36
Character	Exudative	8	15	34
Cavity size (In lysis group prior to operation)	None	2	3	—
	To 4 cm.	7	12	25
	4 to 8 cm.	11	13	40
	8+ cm.	*	19	77
Cavity wall	Thin	8	13	**
	Medium	9	14	26
	Thick	14	12	44
Number of adhesions	Few	4	10	15
	Moderate	7	14	26
	Many	14	13	37

* 3 empyemas in a total of 9 patients.
** No empyemas in 5 cases.

and side were not factors in the empyema rate. Lower lobe disease was present in 14 per cent of the pneumothoraces, and this figure was due to the fact that the hospital admission rate was 4 per cent and to our program of early pneumothorax in this group. Tuberculous bronchitis was present in 24 per cent of a selected group of cases examined. Ultimately 55 per cent of the collapses became successful in closing cavities and controlling the disease. The entire group had pneumothorax for an average of 25 months and an observation period of 45 months.

In the 91 empyemas, 87 patients had a preceding serous or serofibrinous effusion and four cases showed pus from the start. The effusion was "hot" or febrile in 67 per cent. Control of the empyema was accomplished in 64 cases, or 70 per cent; 25 by repeated complete (dry) aspirations, 37 by aspiration plus re-expansion and two by thoracoplasty. The controlled group of 64 patients included seven with bronchopleural fistula, three with pleurocutaneous fistula, and 10 with chest wall abscess. In the uncontrolled group of 27 there were 22 dead at the close of the study and five still alive but with poor prognosis; this group included 11 bronchopleural fistulae, six pleurocutaneous fistulae, 11 with contralateral spreads, and three with chest wall abscesses. Death was due to progression of the disease in the contralateral lung and other viscera and, in three patients, to tuberculous meningitis. The seriousness of empyema is shown by the poor outlook in the 30 per cent which were uncontrolled.

Empyema Factors Inherent in the Pneumonolysis Group

The factors previously discussed included the extent and character of the disease, the size of the cavities, the number of adhesions, and the time of development. Other factors dealing directly with the operation follow.

All the pneumonolyses were done by one operator using the galvanocautery by the double cannula method. In most cases there was need for cutting close to the parietal pleura and considerable parietal stripping; an attempt was made to sever all mediastinal adhesions.

Type of Empyema: In 43 cases the empyema was purely tuberculous, and in five it was mixed, containing also H. Influenza, staphylococcus, streptococcus, and an anaerobic streptococcus. One of these cases was controlled by aspiration and thoracoplasty and one by aspiration and re-expansion; two cases died, and a third is still alive but has a bronchopleural fistula with a poor prognosis.

Cavity Closure: The operation resulted in cavity closure in 127 cases out of the 149 with cavities, or 85 per cent. In this group, there occurred 87 per cent of the empyemas (42 ex 48). In the

unsuccessful cases, the pneumothorax was quickly abandoned or the empyema rate would have been higher. Cavity closure in the pneumonolysis cases did not prevent a high empyema rate.

Pleural Tubercles: In 15 cases, pleural tubercles were seen during the operation and empyema developed in four, or 26 per cent. In no case was a tubercle knowingly traumatized.

Analysis of Table III: The short adhesions resulted in the greatest number of empyemas, but the long ones gave a higher number than the mixed group containing long, medium, and short adhesions and sheets. The thickness of the adhesions was a definite factor, and the thicker they were the higher was the empyema rate. The presence of persistent fluid above the diaphragm gave a high rate of empyema. Only one case with fluid was febrile.

The longer the duration of the pneumothorax prior to the pneumonolysis, the smaller was the empyema rate, and those done after

TABLE III

The Influence Upon the Empyema Rate by the Factors Inherent in the Pneumonolysis Group of Cases

		Number of Pneumonolyses	Resulting Percentage of Empyema
Length of Adhesions	Long	32	31
	Mixed	75	25
	Short	44	43
Thickness of Adhesions	Thin	10	20
	Mixed	79	27
	Thick	62	38
Pleural Fluid Prior to Operation	None	125	28
	Below Diaphragm	12	33
	Above Diaphragm	14	57
Duration of Pneumothorax Prior to the Operation	Up to 3 Mos.	46	43
	3 to 6 Mos.	57	30
	6 to 12 Mos.	33	27
	Over 1 year	15	13
Technical Difficulty	Easiest to do	34	17
	Moderately hard	33	21
	Most difficult	84	41
Technical Results	Good	111	29
	Fair	40	40
	Poor	13	30
Completeness of the Operation	Complete	95	27
	Incomplete	56	39

a year's period produced only one-third as many empyemas as those done early. The average case had pneumothorax for 5.9 months prior to the pneumonolysis. The more difficult the operation the more the resulting empyemas. The better the technical result of the operation (as evidenced by the degree of collapse obtained) the smaller was the number of empyemas. It is to be noted that the "poor technical result" showed a 30 per cent empyema rate—lower than expected—but these cases had early re-expansion of the lung. The more complete the operation the smaller was the empyema rate.

Clinical Estimate of the Difficulty of the Operation: Prior to the operation the routine roentgenograms included postero-anterior and appropriate oblique views (often stereoscopic). In many cases supplementary films were made and included expiratory views, Bucky techniques, planigrams, lordotic views, overpenetrated and underpenetrated exposures. The comparison between the clinical estimate of the probable difficulty of the operation and the actual state of affairs found later follows:

	Clinical Guess	Actual State	Per Cent Error	
Relatively Easy to do	24 cases	34 cases	−30	15
Moderately Hard	54 cases	33 cases	+63	
Difficult	74 cases	84 cases	13	

In the easy and moderate cases combined the clinical estimate was 15 per cent over the actual one. The chief source of error lay in the estimate of the character of the mediastinal adhesions. Thus by careful studies, including fluoroscopy and appropriate films, one can estimate the probable difficulty of the operation in 85 per cent of the patients.

Control of the Empyemas: Full control of the empyemas was accomplished in 32 cases, or 66 per cent; in 16 by repeated "dry" aspirations, and in 15 by "dry" aspiration plus re-expansion of the lung, and one by a Schede thoracoplasty. Of the 16 patients with uncontrolled empyema 12 died chiefly from progression of the disease in the contralateral lung, and eight of these showed bronchopleural fistulae. The four patients still living have a poor prognosis and include three with bronchopleural fistulae. As in the control pneumothorax groups, about one-third of the empyemas are associated with a poor prognosis.

The Time Factor in Empyema Development

Table IV shows the actual empyema rate in the three groups at various time intervals. In the control groups the time is counted from the initiation of the pneumothorax and in the pneumonolysis

TABLE IV

Cumulative Percentage of Empyemas in the Three Groups of Cases

	Effective Pneumothorax 462 cases	Ineffective Pneumothorax 401 cases	Pneumonolysis 151 cases
End of 3 months	1.5	0.5	5.2
4 to 6 months	3.4	2.7	16.5
7 to 9 months	4.7	5.9	23.8
10 to 12 months	5.6	8.7	29.1
13 to 15 months	6.0	10.2	29.1
16 to 18 months	6.7	10.7	29.8
19 to 21 months	6.9	11.4	29.8
22 to 24 months	6.9	11.9	30.4
25 to 36 months	7.7	12.7	31.7
37 to 48 months	8.0	12.9	31.7
Over 48 months	8.4	12.9	31.7

TABLE V

Ratio of Empyemas in the Three Groups (Effective group = 1)

Feature		Effective Pneumothorax 462 cases	Ineffective Pneumothorax 401 cases	Pneumonolysis 151 cases
Extent:	Moderate	1	0.4	1.2
	Far Advenced	1	1.2	3.0
Character:	Exudative	1	1.8	4.2
	Productive	1	0.6	4.2
Cavity size:				Prior to Lysis
	To 4 cm.	1	1.6	3.5
	4 to 8 cm.	1	1.1	3.4
	8+ cm.	(Too few)	1.0	4.1
Cavity wall:	Thin	1	1.7	(Too few)
	Medium	1	1.5	2.9
	Thick	1	0.8	3.1
No. Adhesions:	Few	1	2.5	3.7
	Moderate	1	2.0	3.7
	Numerous	1	1.0	2.6
Time:	End of 3 Mos.	1	0.3	3.4
	End of 6 Mos.	1	0.9	4.8
	End of 12 Mos.	1	1.5	5.2
	End of 18 Mos.	1	1.5	4.4
TOTAL Rate		1	1.5	3.7

group from the time of the operation. At the end of three months (the usual postoperative period) the operated group showed 5.2 per cent empyemas, which is within expected limits for such a group. However, it is only part of a story where the first three months form only the first chapter. In the control groups the rate rises steadily and begins to decline at the end of about two years; in the operative group 90 per cent of the empyemas in this series have occurred at the end of one year.

Figure 1 shows the same data in curve form. The rates are seen to follow a distinct pattern which is similar for the three groups but vary chiefly in height.

Ratio of Empyema Development in the Three Groups

Table V shows the relative ratios of empyemas in the three groups with respect to certain individual factors. In almost all instances the Ineffective group shows a higher ratio than the Effective group. The exceptions are the moderately advanced cases, productive disease, thick-walled cavities, and the first six months

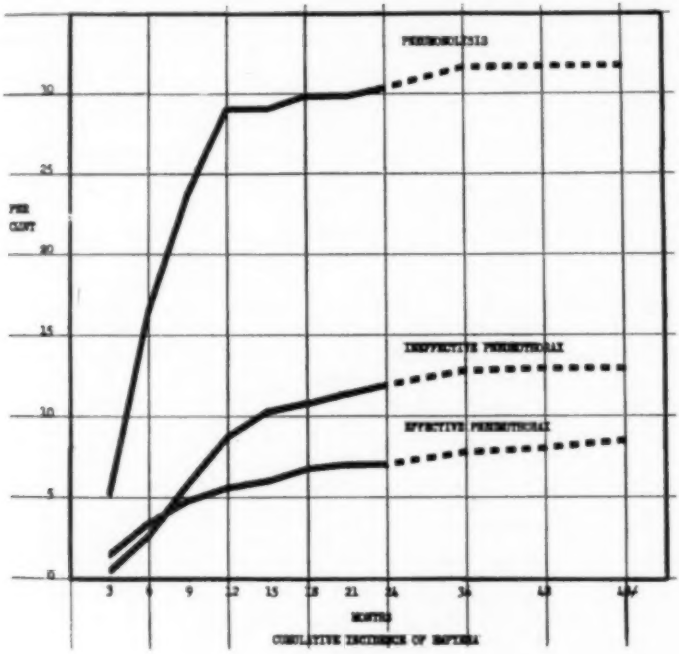

FIGURE 1

of observation. The pneumonolysis group shows a consistently higher ratio in all features mentioned. In general, the total empyema rates in the three groups are reflected in the various individual factors.

The San Fernando Group of Pneumonolyses

Salkin and Netzer[12] made a similar review of the pneumolyses done at the San Fernando Veterans Administration Hospital from 1939 to 1948. All cases with less than a year of pneumothorax were excluded (unless empyema developed previously) to obtain a long range view. No control studies were made.

In this group of 58 pneumonolyses there were 11 empyemas, or 18.9 per cent. Closer analysis revealed that 30 cases could be classified as easy ones technically (less difficult than the Hopemont "easy" group) and there developed two empyemas, or 6.6 per cent. In 13 cases comparable to the Hopemont moderate group, there were two empyemas, or 16.1 per cent; and in 15 cases comparable to the Hopemont difficult group, there were seven empyemas, or 46.6 per cent. Only 54 per cent of the empyemas occurred in the first postoperative year, but all developed within 18 months. The actual empyema rate was 3.4 per cent at the end of the first three months, 5.1 per cent at six months, 10.3 per cent at the end of one year. Thus, the rate of empyema development was several months slower than in the Hopemont group.

Contrary to the Hopemont group the lowest empyema rate occurred when the pneumonolyses were done in the first three months after beginning pneumothorax. However, over 70 per cent of the cases done so early were easy to do and the more difficult cases were deferred until the adhesions appeared more favorable. After the first three months, the rate was constant.

It may be added that fully 13 more cases (or 22 per cent) showed sufficient serofibrinous reaction to thicken the pleural layers considerably, and cause marked encroachment upon pulmonary function.

Discussion

Although the empyema rates for the two pneumothorax control groups do not form the main feature of this study, they present valuable lessons. The empyema figures of 8.4 and 12.9 per cent for the effective and ineffective groups respectively are not unusually high considering the severity of the cases. In the first six months the empyema rate is relatively low (under 3.5 per cent), especially in the non-exudative cases, but at nine months the rise becomes sharp. Thus, one may be fairly safe in taking about six months to make a collapse effective, and there is no need to dis-

continue pneumothorax in only one or two months if it is felt that further collapse may produce a favorable result. The empyema rate can be kept low by the early abandonment of pneumothorax where large cavities and numerous adhesions are present, and where a pneumonolysis might likely result in empyema; by the use of primary thoracoplasty; and by the use of streptomycin to convert a highly exudative lesion to a productive one, either prior to or during pneumothorax.

As commonly believed, the empyema rate is higher in ineffective pneumothoraces than in successful ones. In this study, the rate is 50 per cent higher. This is offset by the fact that the Ineffective group is about 50 per cent more severe. However, since the average ineffective pneumothoraces were only of 13 months duration as opposed to 38 months and since only two-thirds of the empyemas occurred in the first year, the ineffective empyema rate would have been half again as high if the pneumothoraces had been continued as long as the effective cases. The proportion is probably a correct one.

The empyema rates for the control groups follow a definite pattern as shown by their curves. The *pneumonolysis group* presents an empyema curve of a similar pattern but reaches a much higher level. Since this group was not as severe as the Ineffective group, the operation itself must have produced the difference in the empyema rates. Since the rate rises steadily during the entire period of observation, there can be no set time designated as a postoperative period. The only method to obtain a true incidence of empyema in a given series is to compare it over a long term with a control observed at the same time. For practical purposes, the empyema rate may be followed for about 18 months, since over 90 per cent occur during this time.

The high empyema rate following pneumonolysis is due probably to the mechanical and thermal trauma of the operation. The greater and more intense the operative trauma the greater will be the empyema rate. The greater the amount of tuberculous tissue likely to be traumatized, the greater will be the empyema rate as confirmed by the fact that the rate is highest in cases with far advanced disease, with larger cavities, with numerous adhesions, very short adhesions, thickest adhesions, and in cases with unstable exudative disease. The gross and microscopic tubercles in the lung and pleural layers are stimulated to greater activity, which may take some months to become clinically manifest. These factors also are undoubtedly more apparent in the more superficial areas of disease.

It is difficult to explain why the empyema rate in the Hopemont group was less the longer one waited to do the operation, whereas

in the San Fernando group the rate was lowest when the operation was done early. The difference may lie in the groups themselves. The latter was one of chiefly easy pneumonolyses where there was little operative trauma and rapid conversion of an ineffective to an effective pneumothorax. The Hopemont group, however, was a difficult one, and the longer the wait the more the adhesions lengthened, became less vascular, and the exudative disease became more productive.

It must be stressed again that the empyema curves in this study are applicable only to this group of cases designated as difficult pneumonolyses. It is reasonable to assume that the easier the group of pneumonolyses the lower would be the empyema curve and that a very easy group would approximate the control base line. Thus, a simple thoracoscopy should give few empyemas above the basic number expected in a control group, and the number should be especially low if the collapse is abandoned shortly afterwards. The very easy group at San Fernando gave an empyema rate of 6.6 per cent (control figure unknown). The somewhat more difficult groups showed a rate of 16 and 17 per cent; the still harder group showed 21 per cent, and the most difficult groups showed 41 and 46 per cent. Thus, the more difficult the group of pneumonolyses the higher will be the empyema rate above the control base line at that specific time period. It is conceivable that a group of very easy pneumonolyses might give an empyema rate lower than the control group if it causes a more rapid cavity closure and control of the disease.

If a pneumonolysis is expected to be a difficult one and if the factors productive of a high empyema rate are present, then the pneumothorax should be abandoned. A good clinical estimate of such difficulty can be made in 85 per cent of cases, although thoracoscopy should be done in all doubtful cases. The decision to perform a difficult pneumonolysis should be motivated by such strong indications as lower lobe disease where resection is not feasible and thoracoplasty is likely to fail or where bilateral disease prohibits thoracoplasty. And, although empyema can be controlled in two-thirds of the cases, such sequelae as fistulae, thickened pleurae, and severely impaired pulmonary function are so serious that empyema is best avoided. The number of cases with excessively damaged lung function is still higher if one were to add the thickened pleurae resulting from non-purulent serofibrinous effusions. The seriousness of empyema is forcibly impressed when one considers that the 30 per cent uncontrolled cases result in death or a hopeless prognosis.

It is just as important to know when *not* to do pneumonolysis as when to do one. During the operation, the surgeon must again

evaluate the problem if he is presented with a difficult case, adhesions that require much "stripping" or difficult mediastinal adhesions that require division. If a difficult pneumonolysis is done, the pneumothorax should be abandoned in three months if the disease is not being controlled, or if pleural fluid develops. It is not surprising to see the paradoxical phenomenon of an expert surgeon obtaining a higher empyema rate than one less skilled, since the former severs most of the difficult adhesions and the latter only the easy ones.

SUMMARY

1) The incidence of the tuberculous empyema was studied in a group of difficult closed intrapleural pneumonolyses and in two control pneumothorax groups.

2) The pneumonolysis group showed an empyema rate of 31.7 per cent as compared with 8.4 and 12.9 per cent in the control groups.

3) The more important factors contributing to the high rate were the technical difficulty of the operation, the nature of the adhesions, and the nature of the pulmonary lesion.

4) The time of empyema development showed a common curve pattern for all groups. There is no one set time that can be designated as a pneumonolysis postoperative period but an indefinite time limited by the duration of the pneumothorax. For practical purposes a period of 18 months is adequate.

RESUMEN

1) Se estudió la frecuencia del empiema tuberculoso en un grupo de neumonolisis intrapleurales cerradas difíciles y en dos grupos testigos de neumotórax.

2) El grupo de neumonolisis presentó una frecuencia de empiema del 31.7 por ciento, comparado con 8.4 y 12.9 por ciento en los grupos de testigos.

3) Los factores más importantes que contribuyeron a la elevada frecuencia fueron las dificultades técnicas de la operación, la naturaleza de las adherencias y la naturaleza de la lesión pulmonar.

4) El tiempo del desarrollo del empiema mostró una curva común a todos los grupos. No hay un tiempo definido que puede designarse como el periódo postoperatorio de la neumonolisis, sino más bien un periodo indefinido limitado por la duración del neumotórax. Para fines prácticos es adecuado un periodo de 18 meses.

RESUME

1) La fréquence de la pleurésie purulente a été étudiée dans un groupe de sections de brides difficiles et dans deux groupes témoins de pneumothorax.

2) Le groupe où furent pratiquées les sections de brides montra une proportion de 31.7% de pleurésies purulentes, tandis que les groupes de contrôle eurent respectivement un pourcentage de 8.4% et 12.9%.

3) Les facteurs les plus importants qui ont contribué à ces pourcentages élevés étaient la difficulté technique de l'opération, la nature de l'adhérence et l'état des lésions pulmonaires.

4) Le moment du développement de la pleurésie purulente se situe sur une courbe au même point pour tous les groupes. On ne peut pas assigner une limite précise à la période post-opératoire d'une section de bridë. On doit la considérer dans un temps simplement limité pour la durée du pneumothorax. Au point de vue pratique, on peut parler de 18 mois.

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The Place of Pulmonary Resection in the Treatment of Tuberculosis

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Introduction

Within the space of the past few years, pulmonary resection has been accepted as an essential part of any well coordinated therapeutic program in the treatment of pulmonary tuberculosis. The important problem remaining to be solved is the establishment of the proper indications for resection.

The application of any surgical procedure in the treatment of tuberculosis should be based on the safety of the operative procedure and its effectiveness in controlling the disease, Thus, the place of pulmonary resection in the plan of therapy of the tuberculous patient can be determined best by a careful evaluation of two factors: (1) the risk of the operative procedure itself, and (2) the late follow-up of patients who have been subjected to resection. The analysis of these two factors represents the main purpose of the paper.

The risk of resection should be interpreted in the light of present day statistics which have resulted from the application of modern surgical and anesthetic techniques and the use of the protective antibiotics. The administration of streptomycin alone has changed the picture so much that the statistics of even four or five years ago must be recognized as being of only historical interest. The late follow-up will help to determine the effectiveness of resection in controlling the disease and to evaluate how well these patients have withstood the test of time.

Definition of Terms

In the discussion and tables to follow, the postoperative period will indicate the first 60 days following operation; the late period will indicate any time following these 60 days. The pre-strepto-

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mycin era extends from 1934, when the first case was done, to January 1, 1947 when streptomycin became available. The streptomycin era extends from January 1, 1947 to January 1, 1950.

A negative sputum in this report means that the patient is considered to be consistently negative by the physician or institution now caring for him. Because of the wide geographical distribution of these patients, it has been impossible to secure a standard bacteriological examination of the sputum.

Outline of Paper

When possible, the tables and graphs will be self-explanatory. Additional comment will accompany them only when needed to clarify or enlarge on the subject matter and will be located either beneath or on the page opposite the chart. Excessive detail will be omitted intentionally, since the purpose of this paper is to give the overall picture of the resection series without special emphasis on any one phase of the problem.

Scope of Paper

This study represents a careful analysis of 426 tuberculous patients subjected to 437 pulmonary resections between 1934 and January 1, 1950 (11 patients had a second resection). All except two of the living patients have been followed and their present condition evaluated. The following points of special interest shall be emphasized:

(1) *Outline of Indications*
   a. Associated suppuration
   b. Thoracoplasty failure
   c. Predicted thoracoplasty failure
   d. Preservation of function
   e. Elected as operation of choice.

(2) *Comparison of Results in Pre- and Post-Streptomycin Era*
   a. Lobectomy
   b. Pneumonectomy
   c. Segmental resection.

(3) *Analysis of Present Day Risk of Resection*
   a. Lobectomy
   b. Pneumonectomy
   c. Segmental resection.

(4) *Preliminary Report of a Small Group of Segmental Resections.*

(5) *Late Follow-up of Patients*
   a. Pre-streptomycin era — 3 years to 16 years
   b. Post-streptomycin era — 6 months to 3 years.

General Statistics

PULMONARY RESECTION FOR TUBERCULOSIS

1934 to January 1, 1950

Total Resections — 437

Total Patients — 426 (11 patients had 2nd resection)

Operations:

	Pneumonectomy	Lobectomy	Segmental Resection	Total
1934 - Jan. 1, '47 Pre-Strep. Era	152	72	5	229
Jan. 1, '47 - Jan. 1, '50 Streptomycin Era	137	47	24	208
TOTAL	289	119	29	437

Endobronchial Tuberculosis:

	229 Cases Pre-Strep. Era		208 Cases Strep. Era		437 Cases Total	
	No.	Pct.	No.	Pct.	No.	Pct.
Submucosal	18	(8)	20	(10)	38	(9)
Ulcerative	8	(3)	13	(6)	21	(5)
Ulcero-stenosis	18	(8)	14	(6)	32	(7)
Fibro-stenosis	40	(17)	31	(15)	71	(17)
TOTAL	84	(37)	78	(37)	162	(37)

Sex:	No.	*Sputum:*	No.
Female	289	Positive	376
Male	137	Negative	61

Age of Patients:	No.	*Duration of Disease:*	No.	Pct.
3 years	1	Under 1 year	77	(18)
8 years	1	1 to 5 years	213	(49)
15 to 20 years	21	5 to 10 years	77	(18)
20 to 40 years	317	10 to 15 years	40	(14)
40 to 55 years	81	Over 15 years	22	
Over 55 years	16	Survey Lesion	8	

Ipsolateral Lung:		No.	Pct.
(a) No Previous Collapse Therapy		159	(36)
(b) Previous Collapse Therapy		278	(64)
	Pneumothorax 172		
	Phrenic 103		
	Thoracoplasty 104		
	Revision Thoracoplasty 24		
	Lobectomy 11		
	Extrapleural Plombage 2		
	Cavernostomy 8		

Contralateral Lung:		No.	Pct.
(a) Contralateral Disease		183	(42)
(b) Previous Collapse Therapy		34	(8)
	Pneumothorax 32		
	Phrenic 2		
	Extrapleural Pneumothorax 1		
	Thoracoplasty 1		

General Statistics

Comment

1. *Operations:*

Note the increased use of segmental resection during the streptomycin era. This is a reflection to some extent of the increased experience with this procedure gained in treating other conditions, especially bronchiectasis, but also represents an actual widening of the indication for its use in the treatment of tuberculosis.

2. *Sputum:*

The 61 negative sputa occurred in the following groups of patients:

1) Tuberculoma.
2) Bronchiectasis remaining after control of tuberculosis.
3) Non-expandable lungs with bronchial stenosis and/or empyema.
4) Mistaken pre-operative diagnosis.
5) Survey lesions with inadequate sputum studies.

3. *Duration of Disease:*

As would be expected, the majority (49 per cent) of patients had been ill for one to five years. However, 32 per cent had been ill for more than five years and 14 per cent for more than 10 years.

4. *Ipsolateral Lung:*

Note that 64 per cent of the cases represent failures to one or more collapse therapy procedures.

5. *Contralateral Lung:*

Forty-two per cent of the patients had definite contralateral disease (excluding calcified foci) and 8 per cent had had collapse therapy. Many of these had previously had extensive contralateral disease that had undergone resolution. Although most of the contralateral lesions were considered to be stable at the time of operation, a few were definitely active.

6. *Endobronchial Disease:*

In view of the preferential effect of streptomycin on bronchial tuberculosis, it is of interest to note that the incidence of tuberculous bronchitis is exactly the same in the pre-streptomycin and the post-streptomycin eras. Even more surprising is the fact that there has been no essential change in the distribution of submucosal, ulcerative and fibrotic lesions.

RESECTION FOR PULMONARY TUBERCULOSIS
GENERAL INDICATIONS

1. Associated Suppuration.
2. Thoracoplasty Failure.
3. Predicted Thoracoplasty Failure.
4. Preservation of Function.
5. Elected as Operation of Choice.

SPECIFIC INDICATIONS
437 Resections
1934 to January 1, 1950.

	Pre-Strep. Era 229 Resections No. Pct.	Strep. Era 208 Resections No. Pct.	Total 437 Resections No. Pct.
1. Associated Suppurative Disease	20 (9)	14 (7)	34 (8)
2. Thoracoplasty Failure	38 (17)	57 (27)	95 (22)
3. Extensive Unilateral Disease	113 (49)	86 (41)	199 (45)
4. Upper Lobe Disease	30 (13)	24 (11)	54 (12)
5. Basal Disease	19 (8)	18 (9)	37 (9)
6. Tuberculoma	7 (3)	9 (4)	16 (4)
7. Bilateral Giant Cavities	2 (1)	0	2 (0.5)

Comment

It is impossible to list in a categorical fashion the indications for resection since each case must be considered as an individual problem. However, the general indications listed in the table above represent the five criteria used in the Overholt Clinic in accepting patients for resection.

Associated Suppuration:

This is a generally accepted indication for resection and requires no comment.

Thoracoplasty Failure:

(a) Adequate Thoracoplasty

When cavity and positive sputum persist under adequate thoracoplasty collapse, resection has become the procedure of choice unless the respiratory reserve will not permit it. In such cases, cavernostomy and extrapleural procedures are resorted to.

(b) Inadequate Thoracoplasty

When the thoracoplasty collapse is inadequate, revision thoracoplasty or resection can be used. If the residual cavity is large and the chance of failure of revision thoracoplasty is considered

great, resection is the procedure of choice in our clinic. Revision thoracoplasty is reserved for those cases with small residual cavities under a grossly inadequate thoracoplasty.

Predicted Thoracoplasty Failure:

This refers to a group of cases in which thoracoplasty is either contraindicated or offers less chance of control of the disease than a resection, e.g., tuberculoma, associated suppuration, high grade bronchial stenosis, cavities distributed in both upper and basal portions of lung, basal disease, and giant cavities.

Preservation of Function:

At times, resection can be applied with the preservation of more lung tissue and function than when thoracoplasty is used. This is especially true now since it has been demonstrated that segmental resection can be performed in well selected cases with a high degree of safety. The following types of cases fall into this category:

1) Segmental resection of certain types of disease limited largely to one segment.
2) Lobectomy in cases where an open cavity remains in a contracted lobe under pneumothorax.
3) Lobectomy and decortication in preference to extensive thoracoplasty in cases with residual cavity and non-expandable lung.
4) Lower lobectomy in preference to extensive thoracoplasty in uncontrolled lower lobe disease.

Elected as Operation of Choice:

As will be shown later, the mortality and morbidity statistics for lobectomy during the streptomycin era approximate those of thoracoplasty. As a result, the indications for lobectomy are gradually extending. It is frequently used now in preference to thoracoplasty in well selected cases such as those with dense, opaque residual infiltration remaining after treatment with bed rest and antibiotics, those with large to giant-sized cavities, and those with cavities in the superior segment of the lower lobe. In recent months, segmental resection has been used deliberately in many cases who could have been treated by other collapse therapy measures. Present day results justify this approach in well selected cases.

Resection is used more frequently in preference to revision thoracoplasty than it was a few years ago. Extrapleural pneumonectomy as described by Sarot[1] is now considered the procedure of choice in the treatment of cases of empyema with active parenchymal disease.

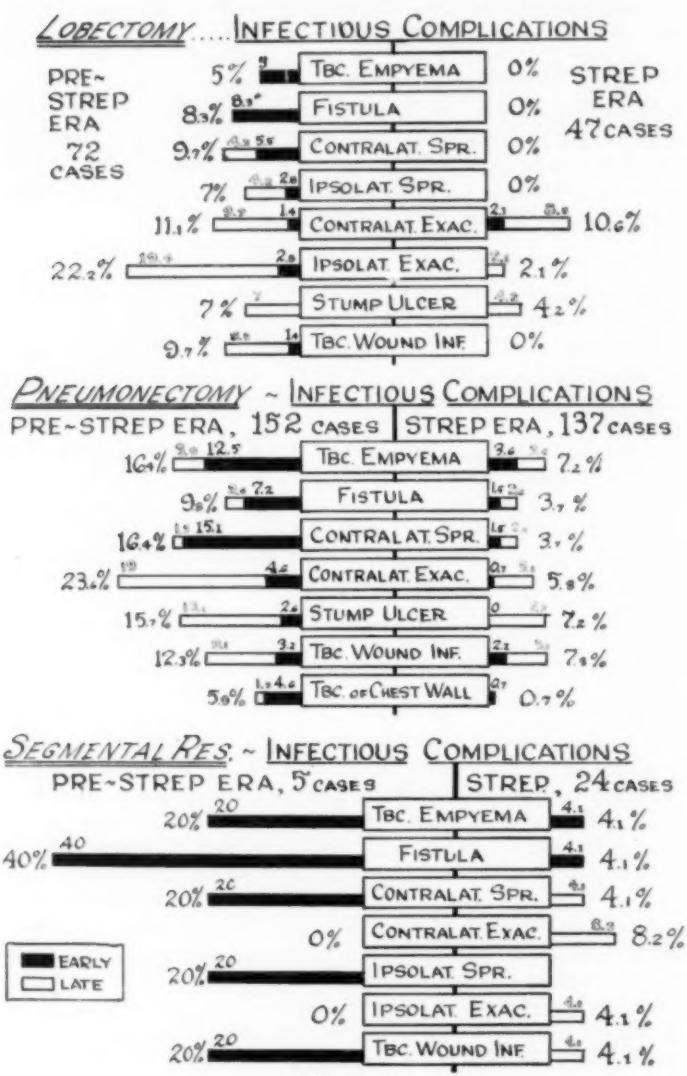
LOBECTOMY.... INFECTIOUS COMPLICATIONS
PRE-STREP ERA 72 CASES
STREP ERA 47 CASES
TBC. EMPYEMA
FISTULA
CONTRALAT. SPR.
IPSOLAT. SPR.
CONTRALAT. EXAC.
IPSOLAT. EXAC.
STUMP ULCER
TBC. WOUND INF.
5%
8.3%
9.7%
7%
11.1%
22.2%
7%
9.7%
0%
0%
0%
0%
10.6%
2.1%
4.2%
0%
PNEUMONECTOMY - INFECTIOUS COMPLICATIONS
PRE-STREP ERA, 152 CASES
STREP ERA, 137 CASES
TBC. EMPYEMA
FISTULA
CONTRALAT. SPR.
CONTRALAT. EXAC.
STUMP ULCER
TBC. WOUND INF.
TBC. OF CHEST WALL
16.4%
9.9%
16.4%
23.6%
15.7%
12.3%
5.9%
7.2%
3.7%
3.7%
5.8%
7.2%
7.3%
0.7%
SEGMENTAL RES. - INFECTIOUS COMPLICATIONS
PRE-STREP ERA, 5 CASES
STREP, 24 CASES
EARLY
LATE
TBC. EMPYEMA
FISTULA
CONTRALAT. SPR.
CONTRALAT. EXAC.
IPSOLAT. SPR.
IPSOLAT. EXAC.
TBC. WOUND INF.
20%
40%
20%
0%
20%
0%
20%
4.1%
4.1%
4.1%
8.2%
4.1%
4.1%

FIGURE 1

Specific Indications:

The specific indications in the 437 cases are listed in the second portion of the above table. Associated suppuration, thoracoplasty failure, basal disease and tuberculoma are well accepted indications for resection in most clinics and represent 43 per cent of the 437 cases. In addition, a high percentage of those with extensive unilateral disease had either associated bronchial stenosis or basal cavities. However, some of this group and the majority of those resected for upper lobe disease could have been treated by thoracoplasty, but resection was elected as the procedure of choice.

Infectious Complications

Lobectomy

Pre-Streptomycin Era:

Eighteen per cent of this group had tuberculous complications in the postoperative period. Empyema and fistula were entirely a postoperative complication, whereas a high percentage of the spreads and exacerbations occurred late.

Streptomycin Era:

Only 2.1 per cent of this group had tuberculous complications in the post-operative period.

Note that tuberculous empyema, fistula, contralateral spreads, ipsolateral spreads and wound infections have been eliminated in the streptomycin period.

There has been no change in the incidence of contralateral exacerbation. In fact, in view of the shorter follow-up period, there may be an actual increase. This may be the result of too much faith in streptomycin and performing lobectomy in the face of an active or recently active contralateral focus.

The marked reduction in the incidence of ipsolateral exacerbation is probably real in spite of the difference in follow-up periods since most of these have become manifest in the first two years.

The incidence of stump ulcer has not undergone any significant change.

Pneumonectomy

Pre-Streptomycin Era:

Thirty-one per cent of this group had tuberculous complications in the postoperative period. Empyema, fistula, and contralateral spread occurred predominantly in the postoperative period. Contralateral exacerbation, stump ulcer and wound infection were more common as late complications. Tuberculosis of the chest

wall refers to infection discovered at the time of post-resection thoracoplasty which had produced no signs or symptoms.

The only tuberculous infections not in the chart were three contralateral pleural effusions and two cases of miliary tuberculosis.

Streptomycin Era:

Only 6.5 per cent of this group had tuberculous complications in the postoperative period. The marked reduction in all complications is evident. The late complications cannot be compared directly, as the follow-up time is so different in the two groups. However, they probably are of real significance, since most of the late complications occur during the first 12 to 24 months.

(Seven non-tuberculous empyemas occurred in the pre-streptomycin era and two in the streptomycin era.)

Segmental Resection

Pre-Streptomycin Era:

This group is so small that it is not of significance statistically. All the tuberculous complications occurred in one patient. One patient had a temporary fistula associated with a non-tuberculous empyema. One other patient had a non-tuberculous empyema that responded to penicillin and did not require drainage. There have been no late complications in this group. All five of these patients are living and well and have a negative sputum.

Streptomycin Era:

Only one patient of the 24 had a tuberculous complication in the postoperative period (fistula and empyema). In the late period there have been one contralateral spread, two contralateral exacerbations, one ipsolateral exacerbation and one wound infection.

There have been no deaths in this group due to tuberculosis. One patient died of a pulmonary embolism. Of the remaining 23 living patients, 21 are well and have negative sputa.

Experience is already demonstrating that the complications of segmental resection depend on the type of case in which it is used. As this procedure is extended in an attempt to salvage cases with bilateral cavities and extensive disease, the complications and deaths can be expected to increase.

Risk of Operation

This graph portrays the risk of the operative procedure separately and also a summary of the statistics for the entire group. The statistical risk of the pre-streptomycin era is given on the left side of the chart. These are of historical interest only and are

presented primarily to serve as a comparison with the statistics of the streptomycin era on the right side of the chart. The figures for the streptomycin era are of real significance since they represent the experience with modern techniques and the use of antibiotics. They should serve as the basis for estimating the risk of operation at the present time.

Comment on Pre-Streptomycin Series:

Sixty-one per cent were carried through the 60-day postoperative period without any type of complication and 73 per cent

RISK OF OPERATION BY %
LOBECTOMY
PRE-STREP = 72 CASES
STREP ERA = 47 CASES
28 TOTAL P.O. COMP. 6.4
18 TB. P.O. COMP. 2.1
4.1 TB. P.O. DEATHS 0
2.8 NON TB. P.O. DEATHS 2.1
6.9 TOTAL P.O. DEATH RATE 2.1
PNEUMONECTOMY
PRE-STREP = 152 CASES
STREP ERA = 137 CASES
44 TOTAL P.O. COMP. 21
31 TB. P.O. COMP. 6.5
7 TB. P.O. DEATHS 0.7
8 NON TB. P.O. DEATHS 5.1
15 TOTAL P.O. DEATH RATE 5.8
SEGMENTAL RESECTION
PRE-STREP = 5 CASES
STREP ERA = 24 CASES
60 TOTAL P.O. COMP. 8.3
20 TB. P.O. COMP. 4.2
0 TB. P.O. DEATHS 0
0 NON TB. P.O. DEATHS 4.2
0 TOTAL P.O. DEATH RATE 4.2
TOTAL RESECTIONS
PRE-STREP = 229 CASES
STREP ERA = 208 CASES
39 TOTAL P.O. COMP. 16
27 TB. P.O. COMP. 5.3
6 TB. P.O. DEATHS 0.5
6 NON TB. P.O. DEATHS 4.3
12 TOTAL P.O. DEATH RATE 4.8

FIGURE 2

without tuberculous complications. Half of the deaths were due to tuberculosis and half to non-tuberculous causes. Both tuberculous and non-tuberculous complications and deaths were more common in the pneumonectomy group. This merely reflects the fact that a more extensive operative procedure was performed on patients with more serious and advanced types of disease.

Although the segmental series is small and percentage of complications high, it is interesting to note that there were no deaths and that all five of these patients are well with a negative sputum at the present time.

Comment on Streptomycin Series:

Eighty-four per cent were carried through the postoperative period without complications of any kind and 94.7 per cent without tuberculous complications (pneumonectomy, 93.5 per cent; lobectomy, 98 per cent; segmental, 96 per cent). The marked reduction in the incidence of tuberculous complications and deaths is very important. In contrast to this, note that there has been no significant decrease in the percentage of deaths due to non-tuberculous causes. Operative shock, cardiovascular accidents, cardiopulmonary insufficiency and pulmonary embolism are now the outstanding causes of death. The total post-operative death rate for the group of 208 cases was 4.8 per cent. Non-tuberculous deaths accounted for 4.3 per cent and tuberculous deaths for 0.5 per cent. The only tuberculous death in the entire series occurred in a 51 year old woman who died of fistula, empyema and disseminated tuberculosis following left pneumonectomy. The one death in the lobectomy group was caused by a contralateral non-tuberculous pneumonia (autopsy). The death in the segmental group was due to pulmonary embolus (autopsy).

Results

Present Status of Patient Analyzed According to Operative Procedure:

This chart analyzes the fate of patients according to the operation employed. The charts are self-explanatory. Results are expressed in percentages. The following points bear emphasis:

Pneumonectomy Group:

The majority of the pneumonectomy patients fall either into the living and negative or dead columns. Only 6 per cent of the pre-streptomycin and 10 per cent of the streptomycin era are in the intermediate classifications.

RESULTS

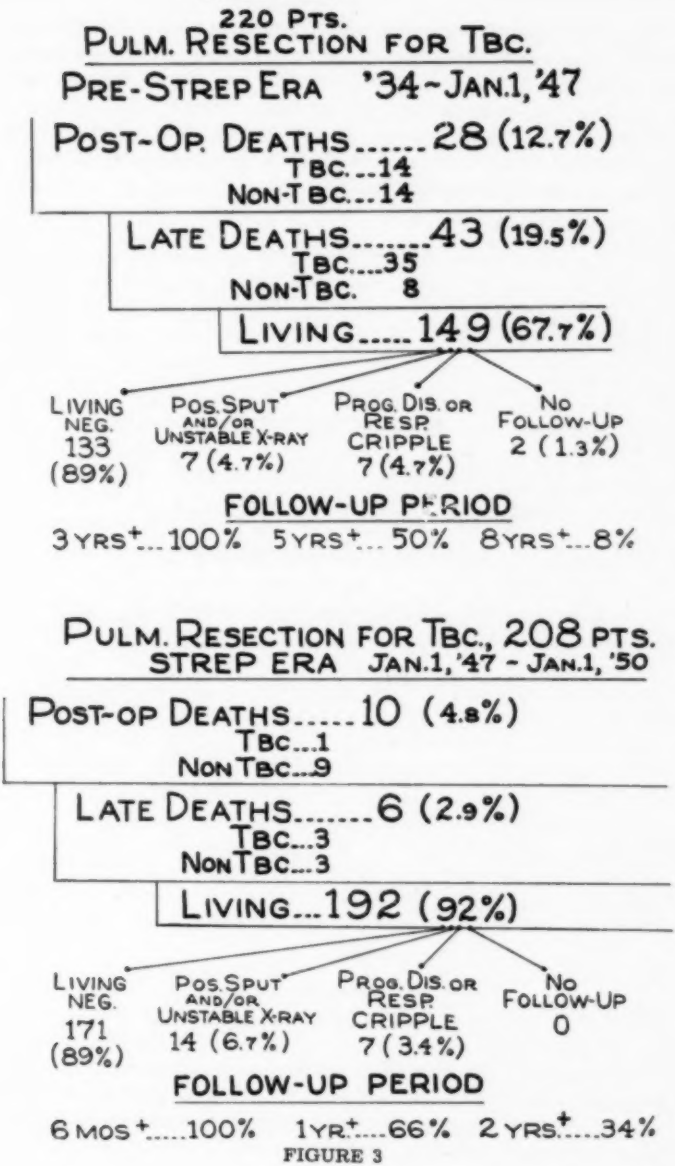
220 PTS.
PULM. RESECTION FOR TBC.
PRE-STREP ERA '34 - JAN. 1, '47
POST-OP. DEATHS 28 (12.7%)
TBC. ..14
NON-TBC. ..14
LATE DEATHS 43 (19.5%)
TBC. ..35
NON-TBC. 8
LIVING 149 (67.7%)
LIVING NEG. 133 (89%)
POS. SPUT AND/OR UNSTABLE X-RAY 7 (4.7%)
PROG. DIS. OR RESP. CRIPPLE 7 (4.7%)
NO FOLLOW-UP 2 (1.3%)
FOLLOW-UP PERIOD
3 YRS+ ... 100% 5 YRS+ ... 50% 8 YRS+ ... 8%
PULM. RESECTION FOR TBC., 208 PTS.
STREP ERA JAN. 1, '47 - JAN. 1, '50
POST-OP DEATHS 10 (4.8%)
TBC. ..1
NON TBC. ..9
LATE DEATHS 6 (2.9%)
TBC. ..3
NON TBC. ..3
LIVING ... 192 (92%)
LIVING NEG. 171 (89%)
POS. SPUT AND/OR UNSTABLE X-RAY 14 (6.7%)
PROG. DIS. OR RESP. CRIPPLE 7 (3.4%)
NO FOLLOW-UP 0
FOLLOW-UP PERIOD
6 MOS+ ..... 100% 1 YR+ .... 66% 2 YRS+ 34%

FIGURE 3

Lobectomy Group:

The percentage of living and negative patients is not significantly greater than in the pneumonectomy group. This is somewhat surprising in view of the fact that lobectomy has been used as a rule in treating less extensive and less serious disease.

As compared with the pneumonectomy group, more of the lobectomy patients fall into the intermediate classifications and distinctly less in the dead column.

Segmental Resections:

This is a small group and represents a more selective series of patients. However, it is extremely interesting to note that of the entire 29 patients only one has died. This was caused by a pulmonary embolus. There have been no tuberculous deaths. All five of the pre-streptomycin series and 87.5 per cent of the streptomycin series are well with negative sputum.

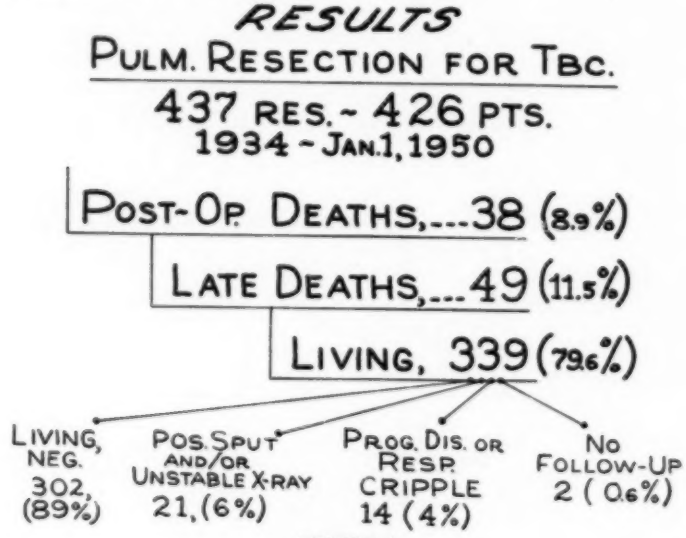
RESULTS
PULM. RESECTION FOR TBC.
437 RES. - 426 PTS.
1934 - JAN. 1, 1950
POST-OP DEATHS, ... 38 (8.9%)
LATE DEATHS, ... 49 (11.5%)
LIVING, 339 (79.6%)
LIVING, NEG. 302, (89%)
POS. SPUT AND/OR UNSTABLE X-RAY 21, (6%)
PROG. DIS. OR RESP. CRIPPLE 14 (4%)
NO FOLLOW-UP 2 (0.6%)

FIGURE 4

Results

This chart presents the results and follow-up statistics of: (a) the 220 patients operated upon prior to 1947 (Pre-Streptomycin Era) and (b) the 208 patients operated upon since 1947 (Streptomycin Era). The incidence and causes of post-operative and late deaths can be compared. The percentage and present status of living patients is also given.

Comment:

1. The post-operative death rate dropped from 12.7 per cent to 4.8 per cent. This was largely due to the marked drop in tuberculous deaths (14 of 28 or 50 per cent in the pre-streptomycin era to one of nine or 11 per cent in the streptomycin era). There has been no significant change in the percentage of post-operative deaths due to non-tuberculous causes.

2. The late deaths are not directly comparable because of the difference in the follow-up period. However, 66 per cent of the streptomycin era patients have been followed for more than one year and 34 per cent for more than two years. In view of this, the marked reduction in late deaths due to tuberculosis is undoubtedly of significance. We believe this is a reflection of the fact that during this time 94.7 per cent of all patients were carried through to post-operative period without a tuberculous complication. In the entire series 77 per cent of the tuberculous deaths, early and late, have been related to or associated with a tuberculous operative complication.

3. The status of living patients likewise cannot be compared directly because of the variation in the follow-up period. However, here again we feel from this study that the marked difference in the percentage of living patients (92 per cent as compared with 67.7 per cent) is due not so much to the effect of time as it is to the fact that 94.7 per cent of those operated upon since 1947 had no post-operative tuberculous complication as compared with 73 per cent in the pre-streptomycin era.

4. The classification of living patients is expressed in percentages of the living patients, not of the entire group. It is interesting that the percentage of living and negative patients is identical in the two groups (89 per cent) and that the distribution in the other classifications is very similar. This also suggests that the follow-up period is not the most significant factor concerned with the status of these patients.

5. The level of activity of the 149 living patients of the pre-streptomycin era, all of whom have been followed for more than three years is as follows:

	No.	Pct.
1. Full Activity	130	(87.2)
2. Graded Exercise	8	(5.4)
3. Bed Rest	9	(6.0)
4. No follow-up	2	(1.3)

6. Although the chart does not reveal it, all tuberculous deaths during the streptomycin era, early and late, have occurred in the pneumonectomy group. There have been no tuberculous deaths in those treated by lobectomy or segmental resection. This is undoubtedly due to more serious types of disease treated by pneumonectomy.

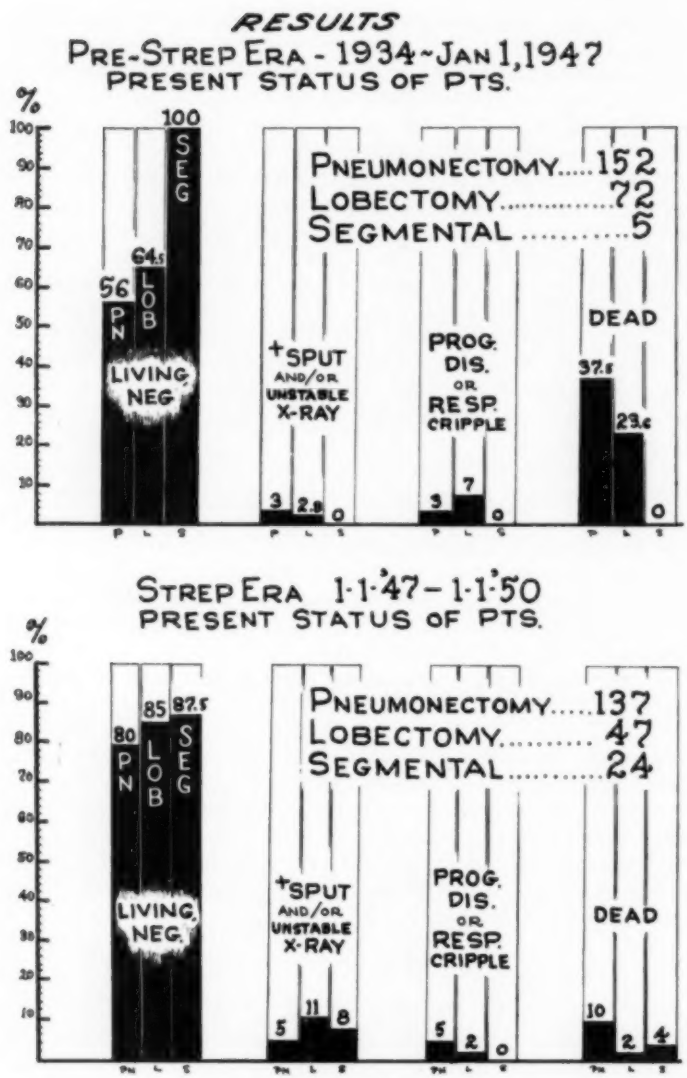
RESULTS
PRE-STREP ERA - 1934~JAN 1,1947
PRESENT STATUS OF PTS.
%
100
90
80
70
60
50
40
30
20
10
56
PN
64.5
LOB
100
SEG
LIVING
NEG
+SPUT
AND/OR
UNSTABLE
X-RAY
3
2.9
0
PROG.
DIS.
OR
RESP.
CRIPPLE
3
7
0
DEAD
37.5
23.6
0
P L S
PNEUMONECTOMY.....152
LOBECTOMY.....72
SEGMENTAL.....5
STREP ERA 1-1-'47 - 1-1-'50
PRESENT STATUS OF PTS.
%
80
PN
85
LOB
87.5
SEG
LIVING
NEG.
+SPUT
AND/OR
UNSTABLE
X-RAY
5
11
8
PROG.
DIS.
OR
RESP.
CRIPPLE
5
2
0
DEAD
10
2
4
PNEUMONECTOMY.....137
LOBECTOMY.....47
SEGMENTAL.....24

FIGURE 5

Results

Entire Series

This chart presents the summary for the entire group of 426 tuberculous patients treated by resection. All except two patients have been followed and their present condition evaluated.

There were 8.9 per cent who died during and 11.5 per cent following the 60-day post-operative period.

Of the entire group, 79.6 per cent (339 patients) are living and of this group 89 per cent are clinically well and have a negative sputum. Ten per cent fall into the intermediate classifications. Some of those with positive sputum and/or unstable x-rays are still salvable. The 14 patients classified as respiratory cripples or with progressive disease are hopeless.

For those who prefer to have all statistics based upon the total number rather than upon the living patients, the following table will be of interest.

	No.	Pct.		No.	Pct.
Total Patients	426				
Postoperative Deaths	38	(8.9)	Dead	87	(20.4)
Late Deaths	49	(11.5)			
Well with Negative Sputum	302	(70.9)	Living	339	(79.6)
Positive Sputum and/or Unstable X-ray	21	(4.9)			
Progressive Disease or Resp. Cripple	14	(3.2)			
No Follow-up	2	(0.5)			

Discussion

During the streptomycin era since 1947 the results of pulmonary resection in the treatment of tuberculosis have improved so much that the statistics of previous years are only of historical interest. In the future, even better results may be expected because of the more intelligent use of streptomycin and the concommitant use of para-aminosalicylic acid. In a large percentage of the cases in this series, sufficient streptomycin had been used prior to surgery to create partial to complete resistance of the tubercle bacilli. However, the prolonged use of the antibiotic was justified in many of these patients because it served to actually save their lives and thus permit them to come to resection. Our experience has been similar to others in that complications were more frequent in those who had had the long courses of streptomycin. However, this is a difficult factor to evaluate because these same patients also had the most extensive and complicated types of disease. In addition, even in these patients the percentage of complications has been low. Regardless of how much drug the patient has re-

ceived prior to surgery, we have given one gram daily for 30 days following resection.*

The results with resection at present permit us to conclude that it represents a relatively safe form of treatment. In fact, the mortality and morbidity rates for lobectomy and segmental resection now approximate those of thoracoplasty. However, we must not be lulled into a false sense of security by statistics. Just because we can perform an operative procedure with a high degree of technical finesse and safety does not necessarily mean that it is the operation of choice. In the majority of cases resection and thoracoplasty should not be competing forms of therapy and thoracoplasty should be used preferentially when there is a reasonable chance that it will succeed. On the other hand, when this reasonable chance of success with thoracoplasty does not exist, resection should be used without a preliminary thoracoplasty, in our opinion. Primary resection is considered the treatment of choice also in those cases in which experience has already proved that the results with resection are superior to those with thoracoplasty and in those with cavities so situated that thoracoplasty would collapse unnecessarily large segments of normally functioning lung.

The success of the major surgical procedures, both thoracoplasty and resection, behooves us to stop and take stock of our therapeutic regimens. Too frequently, treatment is planned according to a routine in which major surgical procedures are used only when other methods, particularly pneumothorax, have been tried and failed. This concept does away with case selection and implies that the simpler measures are either neutral or harmless and in no way jeopardize the patient's future or the success of the major procedures. All too often, however, the simply crushed phrenic and the easily given pneumothorax are likened to the "boy sent out to do a man's job." They fail to control the disease and inevitably rob the patient of a portion, and often too much, of his pulmonary reserve. There can be no doubt that in many instances an ill-advised minor procedure represents a more radical approach than major surgery if we use failure, prolongation of treatment, complications and deaths as our criteria rather than the magnitude of the operation itself.

This is not an incrimination of phrenic paralysis or pneumothorax when indicated, nor the recommendation for the wholesale application of thoracoplasty or pulmonary resection. This is, however, a plea for case selection with the early application of the major surgical procedures when the indication exists.

Only by such individualization of cases can we find the true

*The streptomycin for this work was generously donated by Merck and Company of Rahway, New Jersey.

place for pulmonary resection or any other type of treatment for tuberculosis. Pulmonary resection is a very useful tool, but it is only one of many in our present-day therapeutic "tool box." With the timely and proper use of each of these tools, we can accomplish the goal which physicians all desire and which, in the final analysis, is the true measure of success of any plan of treatment—namely, the return of the greatest possible number of these tuberculous patients to a comfortable, useful and happy life.

SUMMARY

This study represents a careful analysis of 426 tuberculous patients subjected to 437 pulmonary resections between 1934 and January 1, 1950 (11 patients had a second resection). All except two of the living patients have been followed and their present condition evaluated. The following points of special interest are emphasized:

1) Outline of indications.
2) Comparison of results in pre- and post-streptomycin eras.
3) Analysis of present day risk of resection.
4) Preliminary report of a small group of segmental resections.
5) Late follow-up of patients
   (a) Pre-streptomycin era — 3 years to 16 years.
   (b) Post-streptomycin era — 6 months to 3 years.

RESUMEN

Este estudio representa un análisis cuidadoso de 426 enfermos de tuberculosis que se sujetaron a 437 resecciones pulmonares entre 1934 y Enero de 1950 (11 enfermos sufrieron una segunda resección).

Con excepción de dos, todos los demás se han observado y su estado actual se ha evaluado. Es de llamarse la atención sobre los puntos siguientes:

1) Esquema de indicaciones.
2) Comparación de resultados en las pre y post-estreptomicina.
3) Análisis del riesgo de la resección al presente.
4) Informe preliminar de un pequeño grupo de resecciones segmentarias.
5) Observación de los enfermos a largo plazo:
   (a) En la era pre-estreptomicina de 3 a 16 años.
   (b) En la era post-estreptomicina de 6 meses a 3 años.

RESUME

Cette étude représente une analyse très précise de 426 tuberculeux qui ont été soumis à 437 exérèses pulmonaires entre l'année 1934 et le premier janvier 1950 (onze malades eurent un second

temps d'exérèse). Tous les malades encore vivants à l'exception de deux, ont été complètement suivis et leur état actuel précisé. L'auteur insiste sur les points suivants dont l'intérêt est tout particulier:

1) Limite des indications.
2) Comparaison des résultats dans la période antérieure au traitement par la streptomycine et dans la période qui a suivi son utilisation.
3) Examen du risque actuel de l'exérèse.
4) Rapport préliminaire portant sur une petite quantité de malades ayant subi une résection segmentaire.
5) Dernier examen des malades:
   (a) avtn l'époque de la streptomycine, 3 à 16 ans.
   (b) après l'époque de la streptomycine, 6 mois à 3 ans.

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Inhalation Cortisone Therapy in Bronchial Asthma*

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In its original concept, the term "allergy"[1] was used to denote the changed state of the organism that followed the parenteral introduction of an antigen. Although the role of the adrenal corticoids in relation to this altered tissue state is not clear, it appears that in some way they interfere with tissue production of substances which are detrimental to cellular integrity, and thus permit a return to normal cellular homeostasis. This concept offers a rational therapeutic basis for the beneficial effects observed to date in the treatment of acute bronchial asthma with cortisone and/or ACTH.

The predominant pathological findings in bronchial asthma are dilatation of capillaries, edema of the bronchial wall, spasm of bronchial musculature, hyperplasia of goblet cells, and eosinophilic infiltration of the bronchial wall, and peri-bronchial tissue. In addition, thick inspissated mucus plugs are frequently present. Because of the favorable response of allergic inflammatory reactions associated with certain diseases of the eye[2,3] and skin,[4] it was felt that the disturbed tissue alterations of bronchial asthma might be similarly benefited by direct contact with cortisone. The undesirable side-effects and complications[5,6] noted in some instances with other methods of administration of this corticosteroid appeared to make it even more important to investigate this therapeutic approach. It was therefore decided to administer cortisone by inhalation to patients with bronchial asthma, and to compare this method of therapy with parenteral cortisone administration in these patients.

Method and Material

Three patients were selected for study who had been known to have typical attacks of bronchial asthma for eight to 23 years. They were of the male sex, and ranged in age from 29 to 54 years.

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Cortisone was made available through a special grant from the Division of Hospitals, U. S. Public Health Service.

Only one of these patients had a familial history of asthma. All had required frequent treatment with standard methods of therapy, showing transient beneficial response. During a carefully controlled week of hospital observation prior to cortisone administration, these patients continued to show objective and subjective manifestations of bronchial asthma, with intermittent exacerbations of symptoms requiring parenteral use of adrenalin and aminophylline. For two days immediately prior to cortisone administration a placebo solution, consisting of normal saline, was given to two patients by inhalation, four times daily. The use of this inert substance did not alter their symptomatology or clinical course in any way. A saline suspension of cortisone was then administered by aerosol to the patients, one receiving a concentration of 6.25 mg. per cc., and the other two, 12.5 mg. per cc. Each patient inhaled one cc. of cortisone solution four times daily for a two week period. Following this, two patients received 100 mg. of cortisone by intramuscular injection daily for five days. All inhalation administrations were given under standardized conditions,* with oxygen flow regulated at seven liters per minute.

Results

In each of the three patients studied, the administration of cortisone by inhalation was without effect in alleviating the subjective and objective manifestations of bronchial asthma. In two patients, exacerbation of symptoms required occasional parenteral use of adrenalin and aminophylline. This was necessary in one individual despite the administration of cortisone aerosol coincidentally with an acute asthmatic attack.

The patients who received cortisone by intramuscular injection began to experience relief of symptoms within 48 hours, and at the end of four days of therapy demonstrated complete subsidence of all signs and symptoms previously noted. In no instance were any untoward effects of cortisone observed.

Comment

Several recent reports[7,8] have recorded the favorable response of bronchial asthma to cortisone and/or ACTH administration. It is apparent that the use of these corticosteroids in this potentially chronic illness will become more widespread. Although the asthmatic attack may be temporarily controlled, the disease state is not abolished. Because of the observations of the authors[9] and other workers[10,11] of the possible unfavorable effects resulting from the prolonged use of these adrenal corticoids, a method was

*OEM Blue-Dot Bronchial Nebulizer Unit No. 301, with latex rebreathing bag No. 717, Oxygen Equipment Manufacturing Co., Norwalk, Conn.

investigated which might allow their safer use in bronchial asthma. Small amounts of cortisone were administered by aerosol directly to the shock tissue involved. In the cases treated, no beneficial effect was observed in response to nebulized cortisone. The two patients who subsequently received parenteral cortisone demonstrated marked subjective and objective improvement.

Several reasons may be postulated to explain the failure of inhalation cortisone therapy in the cases studied. It is possible that local changes in the bronchial wall due to the long duration of the disease process in these patients prevented proper absorption of the corticoid. True irreversibility of the underlying tissue pathology did not seem to have occurred because of the ability of parenterally administered cortisone to produce profound improvement in these patients. Another possibility is that the bronchospasm associated with the asthmatic state was not relieved by the tissue level of cortisone attained, although the inflammatory changes may have been favorably influenced. It is also possible that in bronchial asthma the action of cortisone is not affected by direct contact at the local tissue level at all, but that a systemic level of the corticoid must be attained to alter the asthmatic state. This hypothesis would seem to be substantiated by the success of nebulized cortisone recorded in a case[12] of bacterial pneumonia, where a satisfactory systemic level was probably achieved by the administration of a total of 313 mg. over a 33 hour period. If it is necessary to attain such levels by aerolization, the possible undesirable effects of parenteral cortisone would not be excluded by this method.

Further investigation is thus warranted before definitive conclusions can be reached, and the final place of inhalation cortisone therapy in bronchial asthma evaluated.

SUMMARY

1) Three patients with long-standing bronchial asthma were treated with cortisone by inhalation, without demonstrable effect.

2) This method of therapy was compared with parenteral cortisone administration in two of these patients.

3) Several reasons are postulated to explain the lack of response to nebulized cortisone in contrast to the favorable response obtained with parenteral cortisone.

4) The observations recorded are the initial results of a continuing study. Further investigation seems warranted.

RESUMEN

1) Tres enfermos con asma de larga duración fueron tratados con cortisona por inhalación sin resultados demostrables.

2) Este método de tratamiento fué comparado con la administración de cortisona por via parenteral en dos de estos enfermos.

3) Varias razones son presentadas para explicar la falta de resultados a la cortisona nebulizada en contraste con los obtenidos por la via parenteral.

4) Las observaciones referidas son los resultados iniciales de un estudio en marcha. Las investigaciones ulteriores están justificadas.

RESUME

1) Trois malades atteints d'asthme ancien ont été traités par inhalation de cortisone, sans effet notable.

2) Pour deux de ces malades, cette méthode a été comparée avec celle de l'administration par voie parentérale.

3) Plusieurs raisons sont invoquées pour expliquer le manque d'action de la cortisone par aérosol en contraste avec l'action favorable de la cortisone par voie parentérale.

4) Les observations mentionnées sont les résultats initiaux d'études qui sont en cours. De nouvelles investigations emblent justifiées.

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Primary Atypical Pneumonia

An Analysis of One Hundred Twenty-Three Cases; Report of One Fatality; Review of Fourteen Cases Treated with Aureomycin.

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The purpose of this paper is to describe the clinical features of primary atypical pneumonia as observed at an Army General Hospital during the first three months of 1949, to report 14 cases treated with aureomycin, and to report the necropsy findings in a patient who died with primary atypical pneumonia. The present series of 123 cases is being compared with 321 cases reported by Painton et al. in 1946.

The clinical material was drawn from a young age group. Fifty-eight per cent of the cases were from 17 to 19 years, with practically all the remainder from 20 to 27 years. It has been the experience of others[16,18] that the disease occurs during the first few months of a recruit's service.

The disease occurs during the entire year but the highest incidence is seen between December and March.

Symptoms: It is generally agreed[2,4] that the onset of this disease is usually gradual with a fairly typical history of five to 10 days duration before the patient is seen in the hospital. Cough, usually non-productive, is the chief complaint, and it is also the first symptom of the disease. Sore throat, fever, malaise, chilliness are next in frequency. Very rarely chills occur two to three days before admission. Frontal headache has been described as a common symptom,[7] occasionally requiring relief by lumbar puncture. However, in this series the occurrence of headache was infrequent. Anorexia, nausea and vomiting are uncommon and are usually presented in a small number of cases who are acutely ill. Blood streaked sputum is rare in this series although it has been noted in one-quarter of the patients reported by Curnen et al.[4]

The symptoms persist a varying length of time following hospitalization. Cough usually becomes productive and is frequently the last symptom to disappear. Fever and malaise persist in few cases. Quite often the roentgenographic picture is the only disturbing feature[10] and several of the cases were asymptomatic and

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afebrile on admission and during the entire hospital stay. About two-thirds of the patients had signs of pharyngitis and about one-half showed some type of rales on auscultation, occasionally fine and moist, but often of a coarse variety that cleared on coughing. It is reported by others[7,18,21] that a transitory inspiratory wheeze is common, however, this was not so in the present series. More common in this series than in others was some change in the character of the breath sounds, either impaired, harsh, or increased in intensity with no one specific character predominating. Fever occurred in almost all cases. The most common experience was a rise of one to two degrees, following admission and then a fall to normal by lysis. Admission temperature in two-thirds of the cases varied between 101 and 103 degrees F.

Laboratory: The expected white cell count in this disease is usually normal and 53 per cent of the present series fall in the range from 5,000 to 10,000. A leucocytosis in excess of 10,000 was found in 35 per cent of the cases and in 12 per cent a count of over 16,000 was reported. Leukopenia was not observed. Differential counts revealed leucocytosis in 79 per cent of the cases as compared with 60 per cent in Painton's series.[18]

In every case in which the red blood count and hemaglobin were estimated, the findings were within normal limits. Urinary abnormalities were not noted. Erythrocyte sedimentation rates were infrequently done and of the 15 reports in this series, two-thirds showed an increased rate up to 38 mm. per hour. In other series the usual experience was a moderate increase of the erythrocyte sedimentation rate.

Serology: The serum of many patients with primary atypical pneumonia develops the property of agglutinating group O erythrocytes in the cold.[9] A positive test is more likely to appear in patients with prolonged or severe illness. Blood for this test should be allowed to clot at room temperature and the serum removed before refrigeration or the patient's own erythrocytes may absorb the substance responsible for agglutination of group O erythrocytes. A positive test usually appears in about 10 days and is present in approximately 50 to 60 per cent of cases tested. A serum titre of 1:40 or more is significant; maximum titres are found during the third to fourth week from onset of the disease, with a diminishing titre thereafter.[9]

The serum of certain patients with primary atypical pneumonia may also develop the property for agglutinating a non-hemolytic streptococcus, called streptococcus M G, isolated from a fatal case. The antibodies are also capable of forming a precipitate with the capsular polysaccharide of streptococcus M G. It has been observed by others[4] that patients who develop this antibody are sicker,

have fever of longer duration, as well as prolonged roentgenographic and physical abnormalities.

Antibodies against streptococcus M G appear between the second and third week and are present at serum titres of 1:20 or more in approximately 50 per cent of patients with primary atypical pneumonia.[9] While some patients may develop antibodies for streptococcus M G and cold agglutinins simultaneously, others will develop one and not the other. Cross absorption tests, one with streptococcus M G that leaves the cold agglutinins intact, two, with group O erythrocytes in the cold, that leave the antibody for streptococcus M G intact, indicates the individual character of the two antibodies.[6]

Pathology: The changes in the lungs consist of an acute interstitial pneumonia uncomplicated by bacterial organisms.[13,17] The bronchioles are filled with a purulent debris and are surrounded by lymphocytes and monocytes. In a case report by McCoy[13] the bronchi contained purulent material and showed irregular ulcerations of the mucosa with thickened walls due to round cell infiltrations. The cellular infiltration extended radially from the bronchi and caused a thickening of the alveolar septa. Most of the alveoli contained a predominantly mononuclear cell exudate. The alveoli become elongated, tortuous and lined with cuboidal epithelium. The general picture is that of interstitial pneumonia and bronchitis. Polymorphonuclear leucocytes are generally absent and it is only with secondary bacterial infection that cells become prominent and fibrin appears.

The mortality resulting from primary atypical pneumonia is low.[8,19] McNeil[15] reports the case of a soldier who died on the 10th day of illness with progressive dyspnea and pulmonary edema. A similar case was reported by Karpel et al.[10] of a 40 year old white male who suddenly, after first showing signs of improvement, became dyspneic, and in spite of oxygen therapy, died after six days apparently of anoxemia.

The following is a case report of a soldier who on admission was not acutely ill, but was found in a semicomatose condition on the morning of the third hospital day.

Case report with necropsy findings: A 25 year old white recruit was admitted on June 27, 1949 with a history of cough and slight expectoration of 24 hours duration.

Physical examination on admission, except for a temperature of 99.2 degrees F., revealed an obese male with no abnormal findings. The white blood count was 17,000 with a normal differential count, red blood count 4,700,000 and hemoglobin 13 gm. Urinalysis was negative; blood urea nitrogen was 28 mgm. per cent, blood sugar 95 mgm per cent, and carbon dioxide combining power 58 vols. per cent.

Chest roentgenogram taken on the day after admission revealed an

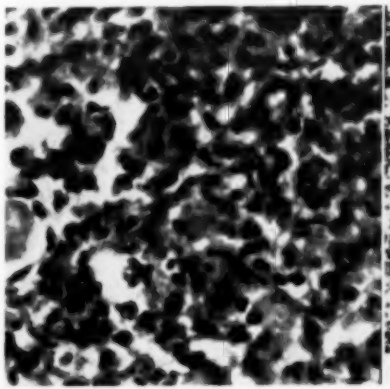

FIGURE 1a

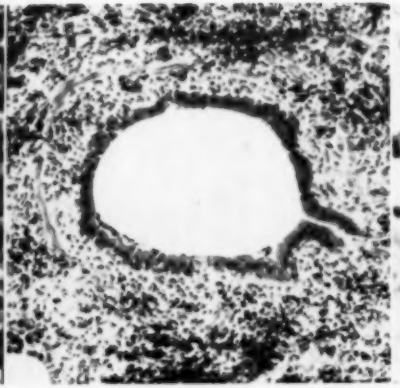

FIGURE 1b

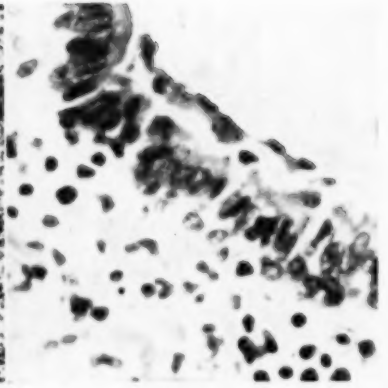

FIGURE 1c

Figure 1a (AFIP No. AC277286-4): A 640x view of the intraalveolar exudate, consisting chiefly of mononuclear cells with few polymorphonuclear leucocytes, from a case of atypical pneumonia. — *Figure 1b* (AFIP No. AC277286-1): A 125x view of a branch of the bronchial tree showing sub-epithelial edema and infiltration by leucocytes, most of which are mononuclear. — *Figure 1c* (AFIP No. AC277286-2): A 640x view of the section shown in Figure 1b.

infiltrate extending laterally from the left hilar region involving the left mid-lung field, and on the right, a mottled infiltrate involving the cardio-phrenic angle. The electrocardiogram was normal.

The patient was not acutely ill at any time, and received only symptomatic therapy. On the morning of the third day, he could not be roused, breathing was labored, blood pressure was 76/40, the lungs were clear on inspiration, though there were many expiratory rhonchi and rales. Oxygen therapy and cardiac stimulants were of no avail, and he expired two hours later.

The essential findings on necropsy revealed an obese male weighing 250 pounds. The lungs were fully expanded and no fluid was found in the pleural cavities. The left lung weighed 500 grams. The visceral pleura was smooth and shiny. The left lower lobe was bluish-red in color and of moderate consistency and was not crepitant. The left upper lobe was light greyish-white in color and crepitant. On cut section, the left lower lobe was moderately firm, there was no exudation of fluid and the bronchi and vessels were grossly negative. Cut section of the left upper lobe revealed air containing parenchyma and appeared to be grossly normal.

The right lung weighed 420 grams. The pleura was smooth and shiny. The middle lobe was bluish-red in color and felt moderately firm. The right upper and lower lobes were light greyish-white in color and felt crepitant. Cut section of the middle lobe revealed moderately firm airless parenchyma. Cut section of the right upper and lower lobes showed grossly normal parenchyma. The bronchi and blood vessels were entirely normal.

The heart was normal, but the aorta was only 4 cm. in circumference. The remainder of the organs were normal. Microscopic examinations of the lungs (Figures 1a, 1b and 1c) revealed scattered bronchioli filled with exudate consisting of mononuclear cells mixed with some polymorphonuclear leucocytes. The peribronchiolar tissues were edematous and infiltrated with lymphocytes and monocytes. In the involved lobes there were scattered areas consisting of thickened alveolar septa engorged with red blood cells, occasional polymorphonuclear white cells, and mainly with lymphocytes, monocytes and occasionally plasma cells.

The microscopic changes in the lungs were reported by the Armed Forces Institute of Pathology as compatible with primary atypical pneumonia with secondary bronchopneumonia, but that many of the finer histological details necessary for an absolute diagnosis of atypical pneumonia have been obscured by the presence of secondary bronchopneumonia.

The spleen revealed hypoplasia of the lymphoid elements and passive congestion; one adrenal showed hypoplasia of the chromaffin tissue, the other was normal. While the necropsy did not reveal the exact cause of death, the microscopic picture of primary atypical pneumonia was found in the lungs of this patient.

Roentgenography: The changes seen on roentgenogram consist of shadows frequently extending out from the hilar regions and appearing as mottled infiltration and areas of increased uneven density of varying size. These changes represent, endobronchial proliferation, peribronchial nodulations, interstitial infiltration, or a combination of all these processes. Occasional small collections

of fluid appear in the interlobar fissures or in the costophrenic angles.[4] Resolution is manifested by thinning of the septa or interstitial tissues, thus enabling the air to be seen again in the lobule;[14] this usually starts first at the periphery and progresses towards the hilum.[2]

The areas involved in this series are compared with the findings of McDonald et al.[14] in Figure 2. Those lesions involving the upper lobe may resemble tuberculosis.[16] There is a distinct predilection for involvement of the lower lung fields with a slight predominance of the left side. Twenty-two per cent of the cases in this series had bilateral lesions either appearing simultaneously or in sequence on follow-up roentgenographic study. Roentgenographic abnormalities disappeared in approximately one-half of the cases within 14 days, and in three-quarters of the cases within 21 days. In two cases, 66 days were required for the roentgenogram to return to normal.

Treatment and Course: Seventy-one per cent of the cases in this series were treated with penicillin, 50,000 units every three hours, during the entire febrile stage. The experience of others[21] has been that sulfonamide or penicillin treatment has not shortened the febrile stage. It should be noted that it is not possible to predict accurately, either the duration or severity of the illness in any given case.[4] In this series 65 per cent of the cases were afebrile by the fifth day and approximately 90 per cent by the 10th day. McDonald,[14] in a series of 75 cases reported that the

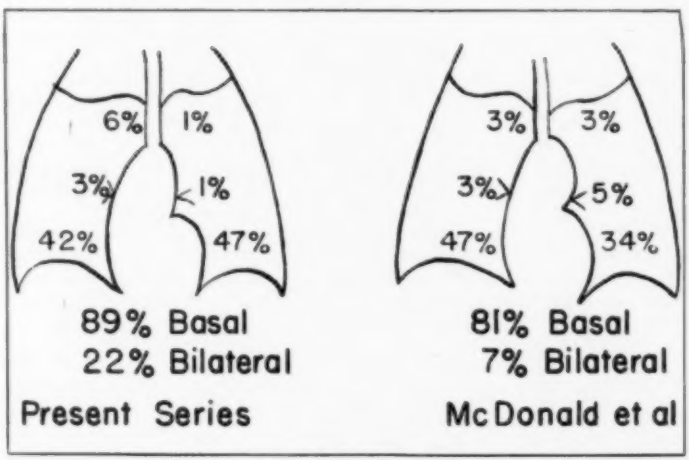

FIGURE 2: Most common sites of involvement of the lung parenchyma as demonstrated by roentgenography.

fever subsided in two to five days by lysis. Almost all our cases were asymptomatic, except for cough, by the time the temperature returned to normal. A few patients complained of asthenia and required further bed rest before convalescence was complete. Persistent cough was treated with expectorants, postural drainage, and occasionally by aerosol penicillin.

The temperature returned to normal in approximately three-quarters of the patients two to three weeks before discharge, which usually occurred when the roentgenogram became normal. The total hospital stay for three-quarters of the patients in this series was up to 30 days with a few remaining as long as two months.

Complications: Five cases not in the aureomycin series, and two of the 14 treated with aureomycin, had exacerbations with fresh roentgenographic findings and recurrence of fever, either just prior to their expected discharge or shortly after. There were two cases with pleural effusion and one on admission had an acute toxic psychosis.

In other series[10,14,18,21] bronchiectasis and lung abscess have been reported as complications of this disease. Bronchiectasis is likely to occur if the course is protracted, and particularly if there is associated roentgenographic evidence of unrelieved atelectasis.[2]

Differential Diagnosis: The following must be considered in differential diagnosis: lobar pneumonia; influenzal pneumonia, characterized by a sick patient with remittent fever, dyspnea, cyanosis, and a productive, frequently bloody, cough; bronchopneumonia; acute exudative tuberculosis; and pulmonary infarction. Psittacosis, influenza A and B, Q fever, and lymphocytic choriomeningitis pneumonia present clinical syndromes almost indistinguishable from primary atypical pneumonia.[9]

Case Reports

Fourteen cases of primary atypical pneumonia seen between the months of January and September 1949, were treated with aureomycin. The response to therapy with aureomycin is comparable in this series to that reported by others.[1,3,5,11,12,20] Following the start of aureomycin therapy symptomatic improvement and a return of the temperature to normal were noted within 18 to 60 hours, and the roentgenographic findings went on to progressive clearing. The average daily dose for the 14 cases was 1.6 gm. of aureomycin in divided doses.

Recurrences, with a return of fever and fresh pulmonary infiltration as seen on the roentgenogram occurred in two patients, 10 days and two weeks respectively, after treatment with aureomycin was stopped. Return to normal occurred on bed rest and

symptomatic treatment. Appearance of fresh roentgenographic findings and return of fever in patients treated with aureomycin for primary atypical pneumonia has been reported by others.[12]

Four case histories with graphic charts and a table summarizing all the cases are presented.

Case 1 (Figure 3) is a 23 year old white male who was admitted with a two day history of non-productive cough, sore throat, fever, and malaise. Physical examination showed temperature of 103.5 degrees F., red and injected pharynx and impaired resonance at the left base posteriorly. He was started on penicillin therapy but continued to have daily temperature elevation to 102 degrees F., with marked general malaise, anorexia and non-productive cough. Chest roentgenogram showed infiltration in the upper two-thirds of the left lung field. On the sixth hospital day, oral aureomycin was started, 0.5 gm. every four hours. Within 16 hours, temperature fell to normal and the patient noted marked symptomatic improvement. On the fourth day of aureomycin therapy, the roentgenogram showed beginning resolution and was completely normal on the ninth day after aureomycin was started. The cold agglutinin titre was found to be 1:40 on the 15th day of the disease. Total hospitalization was 26 days.

Case 2 (Figure 4) is a 20 year old white male who was admitted with a history of shaking chill, and dull ache localized in the left upper chest posteriorly, of 24 hours duration. Physical examination was negative except for temperature of 100.5 degrees F., slight nasal congestion, and pharyngeal injection. Roentgenogram on admission showed increased broncho-vascular markings at the right base and a mottled infiltrate in the right supra-diaphragmatic area, with increase in the amount of infiltration on roentgenogram three days later. The patient was given

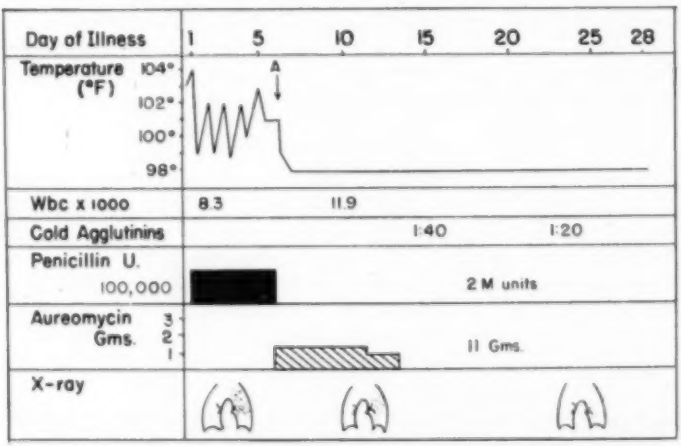

FIGURE 3 (Case 1): Temperature response to aureomycin therapy in 16 hours; marked resolution on chest roentgenogram on the fifth day following institution of treatment.

symptomatic therapy following admission. In view of the roentgenographic findings and a daily temperature elevation of 102 to 103 degrees F., aureomycin 0.5 gm. every four hours was started. Temperature dropped to normal in 36 hours and all symptoms disappeared. Resolution on roentgenogram was noted one week after therapy was stopped. A cold agglutinin titre of 1:5 was obtained on the 13th day of illness. On returning from a week-end pass he complained of headache and general weakness. Roentgenogram at this time revealed a slight increase in the infiltration in the right lower lung field. In view of the fact that he remained afebrile, he was placed on bed rest and symptomatic therapy. Roentgenogram became completely negative in two weeks, and he was returned to duty.

Case 3 (Figure 5): This patient, an 18 year old white male, was admitted with a 24 hour history of left sided chest pain, harsh cough with slight expectoration and fever. Physical examination was negative except for a temperature of 102.6 degrees F. and moist inspiratory rales over the left base, posteriorly. Roentgenogram revealed a mottled infiltrate in the left lower lung field. He was treated with penicillin for six days with no therapeutic response, continuing to run daily temperature elevation of 101 to 102 degrees F. On the eighth hospital day, aureomycin was started, 0.5 gm. every four hours. His temperature returned to normal in 48 hours, however; roentgenogram taken on the fourth day of aureomycin therapy, evidence of pleural effusion was noted at the left base, and therapy was continued for eight more days. Two and one-half weeks after aureomycin was started, the pleural effusion had disappeared and the parenchymal infiltration showed some resolution. The cold agglutinin titre on the 18th day of this patient's illness was 1:160. One week following the onset of resolution at the left base a slight infiltrate was noted at the right base (not shown in Figure 5) accompanied by a moderate amount of expectoration. Roentgenogram returned to normal in 10 days. Total hospitalization was 45 days.

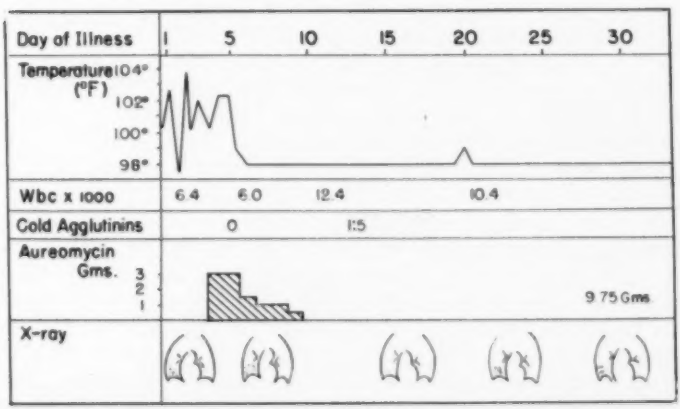

FIGURE 4 (Case 2): Showed initial good response to aureomycin therapy, but following a week-end pass he had a slight clinical exacerbation and a slight increase in pulmonary infiltration.

Case 4 (Figure 6): This 21 year old white male was admitted with a history of cough for one week, productive of small amounts of sputum and associated with slight left anterior chest pain. Physical examination on admission was negative except for a rise in temperature to 103 degrees F. on the afternoon of the day of admission. Roentgenogram on

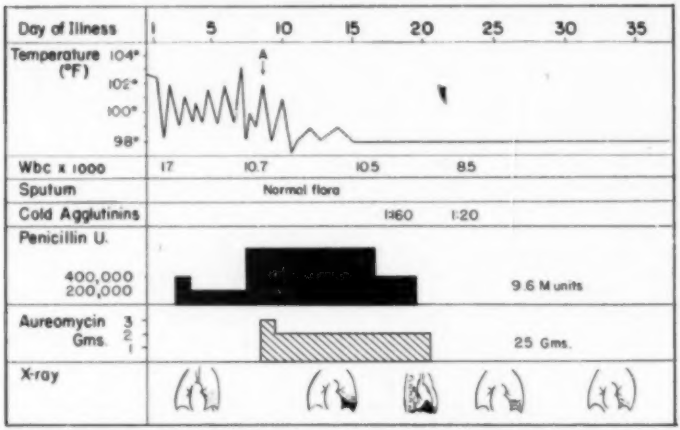

FIGURE 5 (Case 3): Left pleural effusion appeared in this patient on the fourth day of aureomycin therapy.

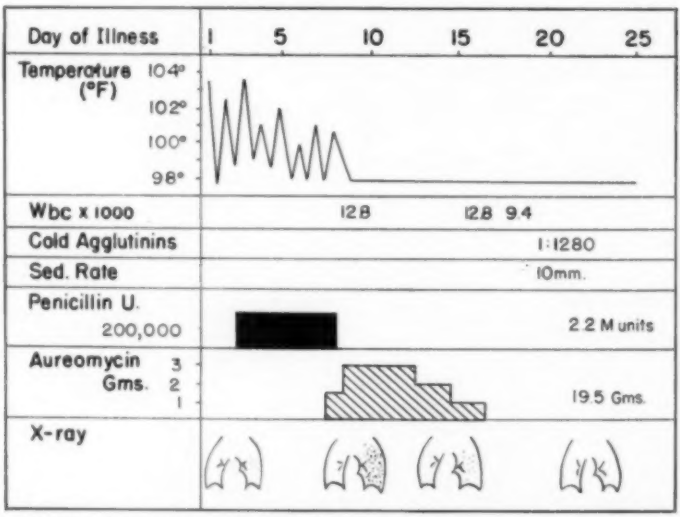

FIGURE 6 (Case 4): At the time of institution of aureomycin therapy, this patient showed marked pulmonary infiltration, was slightly dyspneic and complained of a tightness in his chest.

admission revealed a minimal infiltrate in the left mid-lung field. He ran a daily temperature elevation to 102 degrees F., and on the third day of hospitalization, fine inspiratory rales and inspiratory wheezes were heard anteriorly over the left mid-lung field. He was started on penicillin, but showed no response to this therapy. Roentgenogram taken one week after admission, and at a time when he complained of tightness in his chest and slight dyspnea, revealed a heavy mottled infiltrate involving the entire left lung. He was given aureomycin, 0.5 gm. every four hours, and became afebrile within 16 hours. He noted immediate symptomatic response, disappearance of slight dyspnea and a return of appetite. Repeat roentgenogram on the seventh day of aureomycin therapy showed marked clearing and then complete resolution one week later. A cold agglutinin titre of 1:1280 was obtained on the 20th day of this patient's illness. Total hospitalization was 25 days.

Table I summarizes the 14 cases treated with aureomycin reported in this series. Penicillin was first used in all but one. Continued symptoms and lack of response to bed rest and penicillin were the indications for aureomycin therapy. The total hospital stay was shortened for those cases treated with aureomycin soon after admission.

Comment: Primary atypical pneumonia is a disease seen in a young age group, and in the Army, usually soon after a man comes into the service. The clinical picture starts with cough, and later, fever, chilliness, headache, anorexia, chest pain, and occasionally hemoptysis. Many patients are not acutely ill, although roentgenographic findings may be marked. If fever is present, it usually returns to normal by lysis in five to 10 days. The roentgenogram usually clears in three to four weeks.

Mortality due to primary atypical pneumonia is low. In this series an obese patient died during a bout of primary atypical pneumonia considered clinically to be a relatively mild case. The necropsy findings revealed hypoplastic aorta, hypoplasia of the lymphoid elements of the spleen, hypoplasia of the chromaffin tissue of one adrenal, and pulmonary findings compatible with those previously described for primary atypical pneumonia; however, the exact cause of death was not determined by necropsy.

The patients chosen for aureomycin therapy were more seriously ill than the majority of the patients on whom a clinical diagnosis of primary atypical pneumonia was made. This group of patients before aureomycin therapy was started showed progressive roentgenographic findings, persistent temperature elevation, and no response to bed rest and penicillin therapy. The response to aureomycin therapy seen in these patients was comparable to the results reported by others. In this group of patients cold agglutinin titres were determined in eight cases. A titre of 1:40 or higher was obtained in five out of these eight cases.

TABLE I: CASES TREATED WITH AUREOMYCIN

CASES							— — TREATMENT — —			
Age in Years	Duration of Symptoms Prior to Treatment	Temp. on Admission Degrees F.	Highest Temp. During Hospital Stay	WBC	Cold Aggl.	Lobes Involved	Penicillin (Million Units) Days	Aureomycin Grams Days	Hours for Temp. to Return to Normal	Days in Hospital
No. 1							2.2 units	11 grams		
23 years	2 days	103.5	102	8,300	1:40	LLL	6 days	7½ days	16	26
No. 2								9.75 grams		
20 years	24 hours	100.5	103.5	6,400	Neg.	RLL		5 days	36	43
Remarks: Recurrence with increase in infiltrate RLL 2 weeks after Aureomycin was stopped. Cleared on symptomatic treatment.										
No. 3							9.6 units	25 grams		
18 years	24 hours	102.6	103.5	17,500	1:160	LLL	17 days	12 days	48	45
Remarks: Recurrence with temperature to 101 degrees and infiltrate RLL 10 days after Aureomycin was stopped.										
						LUL				
No. 4						LLL	2.2 units	19.5 grams		
21 years	1 week	103	102	12,800	1:1280	RLL	6 days	9 days	36	25
No. 5							1.2 units	8.75 grams		
20 years	2-3 weeks	104	105.6	7,200	—	LLL	3 days	4 days	33	16
No. 6						RLL	2 units	15.5 grams		
19 years	2 days	101.2	103	7,200	1:5	LLL	5 days	8 days	60	14
No. 7						RUL	10.2 units	17 grams		
17 years	2 days	101	104	6,300	1:80	RLL	21 days	10 days	96	45
Remarks: Aureomycin given when patient became febrile with appearance of lesion in RLL 3 weeks after admission, following 1 week of normal temperature.										

TABLE I: CASES TREATED WITH AUREOMYCIN (Continued)

CASES Age in Years	Duration of Symptoms Prior to Treatment	Temp. on Admission Degrees F.	Highest Temp. During Hospital Stay	WBC	Cold Aggl.	Lobes Involved	— — TREATMENT — — Penicillin (Million Units) Days	 Aureomycin Grams Days	Hours for Temp. to Return to Normal	Days in Hospital
No. 8 17 years	4 days	100.2	103	5,900	—	RLL	4.8 units 8 days	7 grams 7 days	48	23
Remarks: Aureomycin started 12 days after admission.										
No. 9 20 years	3 days	102	103.5	6,700	—	RLL	2.4 units 3 days	12 grams 6 days	36	30
Remarks: No response to penicillin. Started on Aureomycin.										
No. 10 17 years	2 weeks	100	102	14,300	—	RLL	5.7 units 13 days (2 courses)	5 grams 5 days	36	45
Remarks: Aureomycin started when patient failed to improve after two courses of penicillin and almost 4 weeks hospitalization.										
No. 11 18 years	2 days	103.2	103	8,800	—	RLL LUL	1.8 units 3 days	6.25 grams 5 days	24	28
No. 12 18 years	3 days	103	104	9,300	1:160	RLL LLL	1.5 units 4 days	6.75 grams 6 days	60	28
No. 13 17 years	2 days	102	103	10,200	1:10	RLL LLL	0.9 units 3 days	5.25 grams 5 days	24	26
No. 14 20 years	4 weeks	100	103	7,000	—	LLL	1.9 units 7 days	7.6 grams 9 days	18	16
Remarks: Acutely ill with dyspnea, blood-streaked sputum.										

SUMMARY

1) One hundred and twenty three cases with clinical diagnosis of primary atypical pneumonia seen over a three month period, one case history with necropsy findings, and 14 cases treated with aureomycin are reported.

2) The serological, pathological, and roentgenographic findings seen in primary atypical pneumonia are reviewed.

3) Aureomycin has been found to be of definite therapeutic value in treating patients who are acutely ill with primary atypical pneumonia. Temperatures return to normal in 18 to 60 hours accompanied by marked symptomatic improvement. In the few cases observed, resolution of the pulmonary findings on roentgenogram is accelerated, and the duration of hospitalization is shortened. Two cases treated with aureomycin had relapses 10 days and two weeks respectively following chemotherapy; roentgenographic clearing and return to normal occurred on symptomatic therapy in these two patients.

RESUMEN

1) Ciento veintitrés casos con diagnóstico clínico de neumonía primaria atípica se vieron durante un periodo de tres meses. Uno de ellos con necropsia y catorce tratados con aureomicina.

2) Se revisan los hallazgos serológicos, patológicos y roentgenográficos en la neumonía primaria atípica.

3) La aureomicina se ha encontrado de valor definido en los enfermos agudos de este padecimiento. Las temperaturas vuelven a la normalidad dentro de 18 a 60 horas con marcada mejoría sintomático. En los pocos casos observados la resolución radiológica se acelera y se acorta la hospitalización. Dos casos tratados con aureomicina tuvieron recaídas después de la quimioterapia; el aclaramiento radiológico y la vuelta a lo normal concurrieron en estos dos casos.

RESUME

1) Les auteurs rapportent 123 cas pour lesquels le diagnostic de pneumonie primitive atypique a été porté. Ces observations ont été rassemblées pendant une période de trois mois. Dans un cas, ils commentent l'observation et le compte-rendu de l'autopsie; quatorze cas ont été traités par l'auréomycine.

2) Ils font une revue générale des constatations sérologiques, anatomo-pathologiques, et radiologiques de cette affection.

3) L'auréomycine a une remarquable action thérapeutique chez les malades atteints de forme aigue de pneumonie primitive atypique. La température revient à la normale en 18 à 60 heures, en même temps que les symptômes s'améliorent considérablement.

Dans les quelques cas qui ont été observés, il y a eu accélération de la résorption des lésions pulmonaires visibles sur les clichés et le temps d'hospitalisation a été écourté. Deux cas traités par l'auréomycine ont rechuté respectivement 10 jours et deux semaines après ce traitement. Le traitement symptomatique a permis, chez ces deux malades, le nettoyage radiologique et le retour à la normale.

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Primary Anterolateral Thoracoplasty
A Preliminary Report*

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With the elimination of the rib elements of the chest wall, one obtains a caving-in of the soft tissues as a result of which lung collapse is achieved.

Quincke[1] and Spengler[2] are credited with having performed the first thoracoplasties in 1888. Subsequently, Brauer, De Cerenville, Saugman, Tuffier, Sauerbruch, Semb[3] and others introduced changes and modifications in the operative technique. At the turn of the present century Sauerbruch's paravertebral resection of multiple, short rib segments was in general use. Since this operation resulted in an unnecessary sacrifice of large areas of healthy lung tissue, the modern thoracoplasty, in which one resects full lengths of the rib overlying the diseased area, was gradually developed.

It was soon noted, however, that the anterior stumps of ribs were not being removed through the paravertebral incision and Alexander[4] and later Haight[5] introduced an anterior costectomy which was in turn modified by Hedblom[6] using an anterolateral incision. These anterior stages, which find their greatest usefulness in extensive apical cavitation, are performed subsequent to the posterior stages. The development of the former constitute indeed important landmarks in the history of thoracoplasty, although at present they are not universally practiced since, with modern techniques, one can remove the entire rib length through the paravertebral approach.

Our interest in anterior thoracoplasties dates to 1946 when we again turned to the Monaldi operation of transcutaneous cavitary aspiration. At the onset of World War II, in 1942[7] we had reported on our experiences with Monaldi's operation. Subsequent observations showed that failure in this type of treatment resulted from re-inflation of the cavity after discontinuation of suction. To avoid such an occurrence we always felt that if the Monaldi procedure were to be followed by thoracoplasty, cavitary re-inflation would be averted and closure of the lesion assured. Unfortunately, a

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patient who has been submitted to Monaldi's treatment bears on his anterior chest wall a fistulous, tuberculous tract created by the suction catheter; hence, thoracoplasty on such an individual would imply the entering of diseased, tuberculous tissues at the time of the resection of the anterior rib segments. It seemed reasonable, therefore, to invert the sequence of events, performing an anterior thoracoplasty prior to the introduction of Monaldi's catheter. The posterior stage would follow as soon as the aspiration accomplished the obliteration of the tension cavity, without having to invade the area of the tuberculous sinus in the anterior chest wall.

We discovered that the first four patients operated upon according to this plan, tolerated the preliminary anterior rib resection remarkably well. Likewise, we were pleased to note that the posterior stage on these patients who had had partial anterior costectomy of the first four ribs was technically simplified. Thus the idea of performing primary anterior thoracoplasties occurred to us.

Although this plan of treatment was original with us, we can not claim priority for its development, since while preparing the bibliography for this report we have encountered references unknown to us where mention of this technique is made. In "The Collapse Therapy of Pulmonary Tuberculosis" (1937) Alexander speaks of primary anterior thoracoplasty, although only to condemn it. Alexander recommends anterior thoracoplasty as an additional procedure to be used only when the paravertebral operation has failed to produce cavity closure. He insists, therefore, that it is illogical to start thoracoplasty with an anterior

FIGURE 1

FIGURE 2

FIGURE 3

Figure 1: Illustrates patient's position during operation. Incision extends from points A to B.—*Figure 2:* Subperiosteal resection of third rib has been started. Pectoral muscles are well retracted.—*Figure 3:* Average length of ribs resected through anterolateral approach.

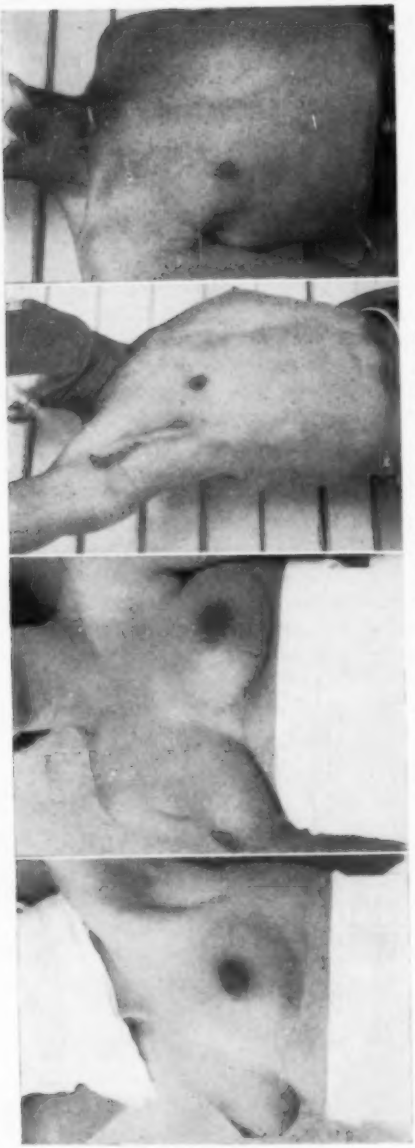

FIGURE 4: Perfect concealment of incision by axillary fold.

stage since, as he rightly states, not all patients will need the latter. In 1928 Duval, Quénu and Welti,[8] as well as Redaelli,[9] reported on their lateral or anterolateral approaches. In 1932 Hudson[10] described primary anterior operation which he combined with a subsequent posterior stage. Based on the statements of Schmidt[12] and Graf,[13] Joachin Hein[11] advocated primary anterolateral stage, but only when the cavities are located anteriorly. R. Finochietto[14] has used the anterolateral thoracoplasty combined with apicolysis which he performs through the interpectoral incision of Vaccarezza; our incision, although similar to the latter, differs in several important respects. In 1945 Sagaz[15] reported on use of the anterolateral thoracoplasty for the control of severe, intractable hemoptysis originating from apical cavities.

Therefore, even though primary anterior thoracoplasty has been mentioned in the literature, it is nevertheless true that its use is far from general. The method has been discussed, but it is seldom employed. We believe that this variation in technique offers definite advantages and that, if not as a matter of routine, it may at least be used profitably in the majority of patients.

Selection of Cases

Our first experiences with this technique were preparatory to the Monaldi operation. We soon became impressed by the smooth post-operative course and by the great tolerance to the operation even among seriously ill patients. Hence, it was a logical step for us to use it in other thoracoplasty candidates whose general condition was precarious, viz: in far advanced bilateral disease, in individuals in the older age group, and in pregnant women. We observed that even the more severaly ill individuals with high degree of toxicity and profuse expectoration tolerated the intervention well; and more important still, their strength and physical condition improved so rapidly that we were able to follow with the required posterior stages much sooner than otherwise.

Subsequently, we decided that if the so-called "poor risks" had satisfactorily tolerated the procedure, the "good risks" should likewise be given the benefit of this milder operation. Hence, at present, practically all our thoracoplasty patients are first submitted to an anterolateral stage which is shortly followed by a paravertebral and final operation. The one exception in which this variation in technique is not employed is in the patient who presents high, small, apical cavities which we feel are still better handled by a single, three to four rib paravertebral thoracoplasty. It would be superfluous to submit this type of patient to primary anterolateral stage since it would by force have to be complemented by a posterior stage for the removal of the posterior rib stumps.

FIGURE 5: Far advanced bilateral case first treated by pneumoperitoneum and streptomycin-PAS before a successful seven rib thoracoplasty was carried out.

To sum up, we advocate that every case with cavernous tuberculosis in which two or more stages of thoracoplasty are contemplated, should have his first operation through the anterolateral approach. By following this rule we widen the scope of thoracoplasty, making it available to a large number of patients who could not possibly tolerate a primary paravertebral thoracoplasty at the outset.

The Intervention

Position: The patient lies flat on his back, with the arm on the operative side in strong abduction, the elbow in flexion and the hand resting under the head. This produces complete relaxation of the pectoralis major muscle (Figure 1).

Anesthesia: We use local anesthesia, complemented by intravenous pentothal sodium when necessary. The skin and subcutaneous tissues are infiltrated with one-half per cent novocaine solution. While lifting the pectoral border with the thumb, we next infiltrate the sub-pectoral space avoiding its superior angle where, because of the proximity to the axillary vessels, annoying hematomas may be formed by blind introduction of the needle. This latter area may be infiltrated subsequently, under direct vision, after the sub-pectoral space is reached. Once the thoracic cage is exposed, the costal grooves of ribs four, three, two and one are infiltrated; this is done as far posteriorly as possible to achieve the most complete anesthesia. We generally use between 150 to 200 cc. of the novocaine solution. A cannula, which has been previously inserted in one of the peripheral veins, is connected to two glass jars by means of a "Y" connection. One of the jars contains normal saline solution and the other 0.2 per cent pentothal sodium solution. The barbiturate is kept in reserve and is only employed when the patient presents nervousness or undue amount of pain, as is usually the case when the actual rib resection is started. When found necessary, we have used from 200 to 300 cc. of the pentothal solution.

Incision: The line of incision follows the postero-lateral border of the pectoralis major muscle (Figure 1). It is about 10 to 15 cm. in length and extends in a straight line from the inferior end of the anterior axillary line (at the level of the fourth anterior rib) to a point 2 cm. short of the intersection of the pectoralis major and the deltoid muscles. It is imperative to prolong the incision superiorly as indicated if we are to obtain an adequate exposure. We believe this incision to be preferable to those employed by Graf, Haight, Hedblom and Vaccarezza, for it results in a much more satisfactory exposure and a less conspicuous scar since most of it is concealed within the axilla. Moreover, there is no limita-

FIGURE 6: Bilateral pneumothorax unsatisfactory; empyema on left yielded to medical management. Preparatory pneumoperitoneum before satisfactory right thoracoplasty.

tion of motion as a result of fibrosis or retraction of the pectoralis major muscle.

Operative Procedure: Upon sectioning the skin and fascia along the described line we find the external border of the pectoralis major. After incising its enveloping fascia and raising the anterior axillary fold, we separate the loose areolar tissue underneath, giving us a clear view of the pectoralis minor. Its tendinous insertions to the second, third, and fourth ribs are easily identified (Figure 2). Using our fingers and sponges on forceps we dissect out the external border of the pectoralis minor, below which and upon its elevation, the axillary portion of the fourth, third and second ribs will become apparent. To localize the first rib we have to dissect bluntly and retract laterally the large vessel-containing axillary fat pad.

The rib resection is carried out sub-periosteally. We find this technique preferable to Finochietto's where the ribs are resected parosteally. We first attack the third rib, incising its periosteum on the presenting rib surface. Using a periosteum elevator we denude the rib over its anterior and posterior surfaces and along its superior and inferior margins. To reach the sternal portion of the rib we tunnel with the elevator underneath the pectoralis minor without having to disturb its tendinous insertions; in similar fashion we strip the posterior portion of the rib. We are thus able to reach as far anteriorly as the costo-chondral junction and, posteriorly, beyond the posterior axillary line. Once the rib has been denuded we first cut it in the center of the presenting arch with a rib cutter; the anterior rib segment is then amputated up to and including part of its cartilage, while the posterior segment is amputated beyond the posterior axillary line. The second rib is treated in a similar fashion.

Because of the deep-lying position of the first rib, it is imperative to thoroughly retract all the surrounding soft tissues. Even then, we will only be able to feel and see a small arc of its anterior border along which, and using the index finger as a guide, the periosteum is incised. We then proceed with the stripping of the periosteum of this rib; this step can generally be carried out with relative impunity, more so than in other forms of thoracoplasty since, due to the extreme abduction of the arm, the costoclavicular space is widened and the sub-clavian vessels are conveniently displaced cephalad. Using blunt dissection and the periosteum elevator we can completely strip away the subclavius as well as the scalenus anticus muscles.

The fourth rib is then sectioned in the same fashion as described above.

In passing, we would like to state that using the described in-

FIGURE 7: Extensive bilateral disease first handled by pneumoperitoneum and six weeks streptomycin course. Eight rib thoracoplasty finally successful.

cision we have been able to section considerably long rib segments. The average lengths of the resected ribs have been 6 cm. for the first, 11 cm. for the second, 16 cm. for the third, and 17 cm. for the fourth ribs (Figure 3).

Once the chest wall has been de-ribbed we generally carry out a partial apicolysis; we never try to approach the extremes of a Semb decollation, especially along the apico-mediastinal region, for fear of obtaining an undesirable drop of the cavity. We only try to produce an antero-lateral, extrapleural pocket which will fill up with sero-sanguinous fluid postoperatively, thus aiding materially in the cavitary collapse.

Two Penrose drains, left in the depths of the wound, are generally removed after 24 hours. These are essential because the violent formation of serum in the created pocket would cause a dehiscence of the wound if an avenue of escape were not provided.

The wound is sutured in layers. In the first plane we suture the borders of the pectoralis major to the areolar tissues of the operative bed. In the second row of sutures the aponeurosis of the pectoralis major is sutured to that of the serratus major and of the latissimus dorsi. This last line of sutures strengthens the wound and helps in the pulmonary collapse since it narrows the chest diameter. The skin is finally approximated by interrupted sutures.

The bandage employed following the operation is a very important detail of the procedure. Even though the de-ribbing is only partial, one generally observes a variable amount of paradoxical motion of the soft infraclavicular and axillary fossae. Corrective measures have to be applied in order to avoid serious complications such as anoxia and retention of secretions. These dangers are averted by external compression with rolled dressings over the above mentioned areas, using two rolls in the anterior and one in the axillary concavities. These dressings are held in place by horizontal, overlapping, tight adhesive bands and by two additional vertical strips which run antero-posteriorly over the shoulder. To further assist in the immobilization of the thorax we employ a shot bag over the operative site. When this bandage is properly applied the paradoxical motion is negligible and we could say that the former is equivalent to an extracutaneous plombage.

All our patients tolerated the operation well and after their recovery we were able to follow with an early posterior stage; technically, the latter is generally quite simple since the anterior two-thirds of the first four ribs has already been resected.

During the paravertebral intervention, besides resecting the remaining posterior stumps of the first four ribs, we also resect full lengths of either three or four additional ribs, depending upon

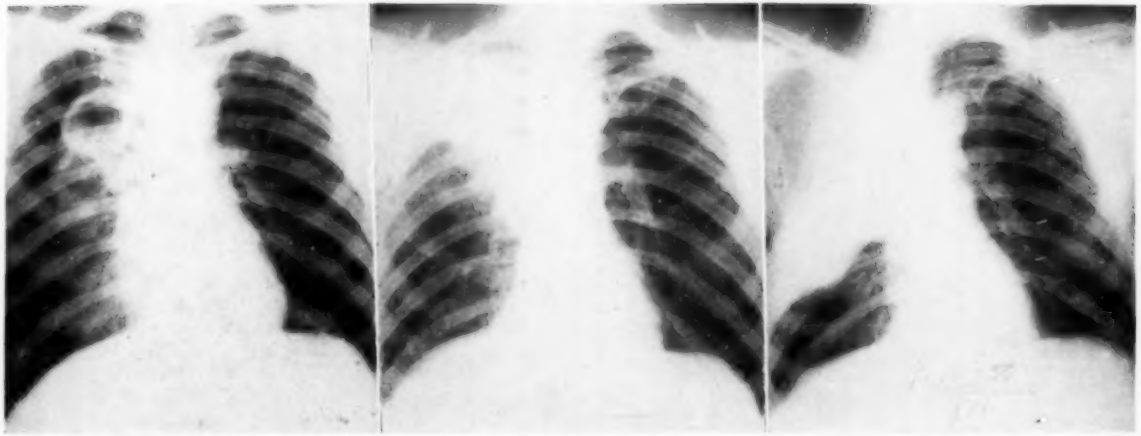

FIGURE 8a FIGURE 8b FIGURE 8c

Figure 8a: Multiple right lung cavitation with unsatisfactory pneumothorax in a four month pregnant woman.—*Figure 8b:* Three-rib anterolateral stage.—*Figure 8c:* Six-rib thoracoplasty satisfactorily completed.

the extent of collapse required by the pulmonary lesion. We invariably and intentionally break into the decollated pocket created during the first operation, thus obtaining an almost complete collapse of the upper lobe as the apicolysis is extended posteriorly. Because of this fact, primarily, we advocate an early posterior stage, preferably within the first 15 days after the anterolateral intervention. If the interval between stages were prolonged, the second operation would be technically more difficult and the apicolysis would be less complete and anatomically less perfect due to the bony regeneration.

Results — Complications

To-date, 24 patients have been operated upon according to this technique. Of these, six were thus treated in preparation for a Monaldi procedure; hence, they will not be included in this report. Besides, three still await their final paravertebral stage. Therefore, there are 15 patients on whom the planned rib section has been completed.

Of these 15 patients, three were strictly unilateral and 12 bilateral. Of the latter group three had concomitant pneumoperitoneum, one a contralateral pneumothorax, one, obliterated and cured contralateral empyema, and one was four months pregnant. Amongst the 15 patients 12, or 80 per cent, have turned negative. We wish to point out that our criterion of negativity is now stricter than it had been in the past months; a patient must now have negative cultures of sputum, gastric and/or bronchial washings, before he is considered negative. We believe it is a mistake to call a patient negative unless cultures or animal inoculations are carried out. Hata and his associates[16] have recently presented corroborating evidence to this effect.

Of the three patients who are still positive, only one shows an open lesion, a tension cavity with complicating bronchial disease for which pneumonectomy had been proposed and refused. In the other two cases we have achieved cavity closure as demonstrated by tomography and they may possibly turn negative at a future date.

All our patients have been remarkably free of complications. We have had no recent or late deaths. We have had no wound infections, no uncontrollable paradoxical breathing, no retention of bronchial secretions, no contralateral spreads and no reactivation of contralateral arrested lesions. One developed locking of the angle of the scapula, which was successfully treated by partial scapulectomy elsewhere. Another developed painful protrusion of an anterior cartilage stump, which was satisfactorily managed by amputation during the posterior stage.

Discussion

The variation in technique presented here offers unquestionable advantages over the classical paravertebral operation. With the anterolateral approach we avoid sectioning of heavy muscles, untoward paradoxical motion of the chest wall, mediastinal flutter, and post-operative shock. It allows us to proceed with greater speed and to operate on patients with low exercise tolerance.

Our pregnant patient is a case in point; she was extremely dyspneic and presented profuse expectoration. The anterolateral partial resection of three ribs was carried out with a remarkable improvement of her vital signs. Fifteen days later we followed with a paravertebral operation, at which time the posterior stumps of the first three ribs, besides three entire additional ribs, were removed. Had we used the classical procedure on this girl, we would have been forced to perform her thoracoplasty in multiple, small stages, thus increasing the risk to both mother and child. This patient was safely delivered at term by Cesarian section because of maternal dystocia.

The use of ligature material is considerably diminished with this technique, since we reach the costal cage through blunt and anatomical dissection. The operation itself is esthetic, the incision is small and it is mostly hidden in the axilla, excessive blood loss is avoided, and there is a minimum amount of shock-producing mutilation. We have not found it necessary to employ transfusions after the anterolateral stage.

We wish to stress the importance of performing the posterior intervention within the first 15 days after the anterior stage, if we are to prevent the loss of collapse which results from the rigidity and osseous regeneration at the operative site. Moreover, by avoiding delays, the posterior stage is definitely facilitated, especially with respect to the removal of the posterior rib stumps.

It is not always possible to perform the posterior intervention in one stage. One of our patients revealed respiratory difficulties after the removal of the sixth rib, making it necessary to postpone the resection of the seventh and eighth until a later date. Another had to have a revision of the thoracoplasty with removal of the ninth rib, which was naturally performed through the posterior apprach at a third sitting. In all other patients, however, we were able to perform six, seven or eight rib thoracoplasties in the two described interventions.

To a large extent our success has been due to the close cooperation we have received from our internists. They have known how and when to make intelligent use of pneumothorax, pneumoperitoneum and antibiotics, thus converting bilateral, inoperable indi-

viduals into cases with controlled disease in one lung and operable lesions in the other. The strategic use of streptomycin, limiting its use to short, 42-day courses or to the pre- and post-operative periods, has given us the protection of this valuable drug during the operative crisis. The erratic use of streptomycin should be condemned, especially when applied in long and futile courses which invariably make the bacilli resistant to the drug and rob the patients of the advantages of a truly life-saving drug during the risks of the operation.

Thoracoplasty is definitely established as a method of collapse therapy of unquestionable value. Statistics show that modern thoracoplasty techniques offer progressively better results, not only from the point of view of symptomatic improvement, but also from the point of view of permanency of cure. We believe that the changes in technique offered above help to eliminate many of the objections that have been raised against the procedure.

SUMMARY

1) We have presented a new concept in the performance of thoracoplasty for pulmonary tuberculosis. A history of the development of the method is given.

2) Primary, anterolateral, sub-pectoral resection of the anterior portions of the first four ribs is first carried out; this is followed within 15 days by a paravertebral operation in which the remaining posterior segments of the first four ribs, and three or four additional entire ribs, are removed.

3) We advocate the routine use of this operation in all cases in which two or more stages of thoracoplasty are contemplated. On the other hand, the patient with a small apical cavity who usually responds to a single three or four rib upper thoracoplasty should not be submitted to our anterolateral, primary stage.

4) A detailed description of the position, anesthesia, incision, operative procedure and bandage used has been given.

5) The following obvious advantages of the method may be mentioned:

a) It allows us to operate on patients with poor exercise tolerance, through an inconspicuous incision and with greater rapidity and safety.

b) It diminishes the number of operative interventions without sacrifice in the circumferential collapse.

c) It facilitates the performance of the second, posterior stage.

d) Avoidance of muscular section, paradoxical respiration, retained bronchial secretions, mediastinal flutter, post-operative shock, excessive use of suture material, excessive blood loss and post-operative transfusions.

6) We believe the method suggested merits a trial, and if found worthy its use should become general.

RESUMEN

1) Hemos presentado una nueva modalidad en la técnica de la toracoplastia. Se hace una reseña histórica del desarrollo del método.

2) Se practica de primera intención una resección primaria, anterolateral, subpectoral de los extremos anteriores de las cuatro primeras costillas, seguida dentro de los próximos quince días de una intervención paravertebral en la que se resecan los muñones posteriores restantes de las cuatro primeras costillas, además de tres o cuatro costillas completas adicionales.

3) Abogamos por su uso en todo enfermo a quien se le anticipen practicar dos o más tiempos de toracoplastia. Es innecesaria en aquellos que presentan cavernas pequeñas, apicales, las cuales generalmente son suceptibles a una sesión de toracoplastia por vía posterior de tres o cuatro costillas.

4) Se describe la intervención en todos sus detalles.

5) Se apuntan las ventajas de este método entre las que se destacan, disminución en el número de intervenciones sin sacrificar el excelente colapso circumferencial, ausencia de sección muscular, facilidad de la técnica operatoria incluso en la sesión posterior, tolerancia perfecta a la intervención aún en los casos más graves, colapso adecuado de las cavernas y ausencia completa de complicaciones.

6) Se evita la respiración paradójica, el bamboleo mediastínico, el shock post operatorio, el uso excesivo de material de sutura, la pérdida de sangre excesiva, las transfusiones postoperatorias y la retención de secreciones en el árbol bronquial.

7) Creemos conveniente el empleo y la difusión del método.

RESUME

1) L'auteur a établi une nouvelle conception de la thoracoplastie pour tuberculose pulmonaire. Il donne l'historique du développement de cette méthode.

2) Tout d'abord la résection antéro-latérale sous-pectorale des extrêmes anterieurs des quatre premières côtes est réalisée. Le deuxième temps suit quinze jours après, et consiste à supprimer par voie para-vertébrale les fragments restants des 4 premières côtes et trois ou quatre côtes de plus en totalité.

3) L'auteur propose l'utilisation habituelle de cette opération dans tous les cas pour lesquels on envisage au moins deux temps de thoracoplastie. En d'autres termes, le malade qui est porteur d'une petite cavité apicale pour laquelle une thoracoplastie de

trois ou quatre côtes en un temps est indiquée n'est pas justiciable de cette technique.

4) L'auteur donne une description détaillée de la position du malade, de l'anesthésie, de l'incision, du procédé opératoire et des pansements.

5) Il faut mentionner certains aventages évidents de cette méthode:

a) elle permet d'opérer des malades peu tolérants à l'aide d'une incision peu visible, et avec les plus grandes rapidité et sécurité.

b) elle diminue le nombre des temps opératoires sans diminuer le collapsus circonférentiel.

c) elle facilite la réalisation de second temps postérieur.

d) elle évite les sections musculaires, la respiration paradoxale, la rétention bronchique, le balancement médiastinal, le choc post-opératoire, l'utilisation excessive de matériel de suture, l'hémorragie trop abondante et les transfusions post-opératoires.

6) L'auteur pense que la méthode qu'il conseille mérite d'être essayée, et si elle est satisfaisante, elle pourrait être généralisée.

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The Surgical Pathology of Pulmonary Tuberculosis*

Mechanism of Cavity Healing as Seen with Streptomycin Therapy

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Lung tissue, removed surgically in pulmonary tuberculosis, offers for study a stage in the pathology of the disease seen only fortuitously at autopsy before the perfection of surgery. Reports on pulmonary resections have stressed surgical technique, indications, contraindications, and results. Descriptions of the specimens removed have been included, to supplement the clinical story, frequently with some pathological discussion.[1-3] A clinical and pathological correlation of resection material has been reported by Fujikawa and Ackerman[4] and the pathology seen in the surgical specimens has been studied by Meissner,[5,6] Buckles and Neptune,[7] and by Mahon.[8] To date a wide diversity of cases have been presented, many of the reports dealing, in part, with pneumonectomies or lobectomies of fibrosed lung, in which the pathology was advanced.

With the recent development of segmental resection,[9,10] and the resultant elimination of the needless loss of functioning parenchyma, surgical intervention has become a more frequent elective procedure early in the course of the disease. At Triboro Hospital, segmental resection is, in many instances, chosen in preference to a long standing trial by thoracoplasty; the purpose being simply to remove a seeding focus of tuberculosis, usually a cavity, with preservation of maximum function. Lateral tomography is utilized in the localization of lesions. An attempt is made to intercede surgically at the optimum time when the patient's healing processes balance, to some degree, the progress of the disease. Streptomycin used preoperatively helps the patient attain this optimum level. It is to be expected, therefore, that the study of such surgical specimens may clarify some of the concepts of the pathology of tuberculosis. The following is a report on an unselected number of consecutive resections, excluding pneumonectomies, done within an approximately six month period at Triboro Hospital.

*From the Department of Pathology and Thoracic Surgery of Triboro Hospital, Jamaica, New York.

Material Used

Twenty-two specimens were studied. These included eight lobectomies, 12 segmental resections, and two instances in which both a lobectomy and resection of a segment of the adjacent lobe were done. Since tuberculous cavities tend to be found in the costovertebral gutter, the portions of lobes resected were usually apical and posterior segments of upper lobes or the apical segment of a lower lobe. Table I presents the sex, age, race, and preoperative therapy used in each of the cases.

Since, as mentioned above, the purpose of surgical, particularly segmental, resection was to eliminate one or more foci of tuberculosis which served as the points of origin for dissemination, the majority of the specimens presented cavity formation. Cavities were seen in various stages of development, from open cavities with patent bronchi to encapsulated caseous foci, with grossly blocked bronchi. In two instances cavities were apparently represented almost entirely by scar tissue.

The 22 cases were subdivided according to the degree of regression or healing presented by the cavitation in each specimen. If a specimen showed evidence of more than one cavity it was classified according to the most active lesion found. The cases fell into four groups:

Group I: Cavity, with draining bronchi patent grossly and tuberculous. Cases one to nine inclusive.

Group II: Cavity with draining bronchi blocked grossly, or only one found patent grossly. The majority of the draining bronchi were tuberculous. Cases 10 to 15 inclusive.

Group III: Cavity, with draining bronchi blocked grossly and not tuberculous. Cases 16 to 20 inclusive.

Group IV: Probable cavity, represented for the most part by scar tissue. Cases 21 and 22.

It is obvious that the groups tend to merge. A grossly patent bronchus might have been overlooked. The "blocked" bronchi of group II prevented the passage of a probe, 1 mm. thick, but many showed microscopic patency. Adequate investigation of cavities and their draining bronchi requires detailed study with almost serial sectioning. Numerous blocks were cut from each case, but a tuberculous involvement of a bronchus could have been missed.

In each specimen, the following points were studied:

1) The cavitation, for size and content. 2) The bronchi draining the cavity, for patency and the presence of tuberculosis. 3) The bronchi in the lung parenchyma some distance removed from the cavity, for the presence of tuberculosis. 4) The disseminated foci. 5) Both the hilar bronchial and parenchymal planes of

TABLE I

CASES STUDIED

Case	Sex	Age	Race	Duration of Disease Preop. in in Years	Previous Collapse Therapy	Courses of Streptomycin Therapy	Resection
1	F	24	W	7	None	25 gm. preop.	Lobectomy, RUL
2	M	32	W	7	Rt. pnthx.	1) 40 gm. 2) 37 gm. preop.	Lobectomy, RUL Segmental, apex RLL
3	M	25	W	3	None	1) 40 gm. 2) 36 gm. preop.	Segmental, apex RLL
4	F	32	W	10	Bilat. pnthx.	1) 40 gm. 2) 135 gm. preop.	Segmental, LUL
5	M	49	C	2	None	5 gm. preop.	Lobectomy, RUL
6	F	32	C	7	Lt. pnthx.	18 gm. preop. with PAS	Segmental, apex LUL
7	F	45	W	7	Bilat. pnthx. Pneumoperit. Rt. thoracopl. preop.	1) 42 gm. 2) 42 gm. 3) 30 gm. preop.	Lobectomy, RUL
8	F	43	C	1	None	1) 42 gm. 2) 30 gm. preop.	Lobectomy, RUL
9	M	37	W	11	Bilat. pnthx.	14 gm. preop.	Segmental, LUL
10	M	42	W	10	Lt. thoracopl. preop.	15 gm. preop. with PAS	Segmental, apex LLL
11	M	23	C	7	Bilat. pnthx.	1) 42 gm. 2) 42 gm. 3) 36 gm. preop.	Segmental, apex LUL

TABLE I

CASES STUDIED (Continued)

Case	Sex	Age	Race	Duration of Disease Preop. in in Years	Previous Collapse Therapy	Courses of Streptomycin Therapy	Resection
12	F	33	W	4	Lt. phrenic crush	1) 42 gm. 2) 48 gm. preop.	Segmental, LLL
13	M	23	W	1	Rt. pnthx.	1) 45 gm. 2) 37 gm. preop.	Lobectomy, RML
14	M	18	W	4	Rt. pnthx.	1) 37 gm. 2) 42 gm.	Lobectomy, RUL
15	F	41	W	¾	None	1) 42 gm. 2) 37 gm. preop. with PAS	Segmental, apex LUL
16	F	28	W	5	None	40 gm. preop.	Segmental, apex LUL
17	F	25	W	2	None	1) 42 gm. 2) 36 gm. preop.	Segmental, apex RLL
18	M	38	W	6	Lt. thoracopl. preop.	1) 42 gm. 2) 54 gm. preop.	Segmental, LUL Segmental, apex LLL
19	M	52	W	1½	None	1) 42 gm. 2) 21 gm.	Lobectomy, RUL
20	F	27	W	9	None	1) 42 gm. 2) 51 gm. preop. with PAS	Lobectomy, RUL
21	F	28	W	8	Rt. thoracopl. 5 yrs.	29 gm. preop.	Lobectomy, RUL Segmental, apex RLL
22	F	25	W	1	None	27 gm. preop. with PAS	Segmental, apex RUL

FIGURE 1

FIGURE 2a

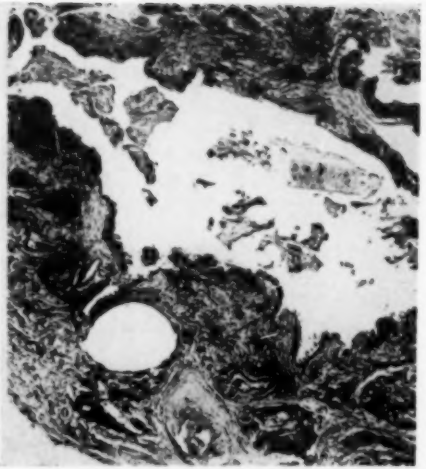

FIGURE 2b

Figure 1, Group 1, Case 2: Resected right upper lobe and apex of right lower lobe. Large cavity is present in the apex of the right lower lobe; draining bronchi adjacent to cavity are tuberculous, patent, some filled with caseous debris. Spherical caseous foci in the upper lobe represent cavities.—*Figure 2a, Group 1, Case 8:* Resected right upper lobe with small open cavity. Draining bronchi patent and tuberculous. Note lack of appreciable caseous content in cavity in this case.—*Figure 2b, Group 1, Case 8:* Tuberculous ulceration of patent draining bronchus, seen below cavity of Figure 2a.

resection, for the presence of tuberculosis. Table II is a tabulation of the above findings in each of the cases.

Discussion:

This report is mainly concerned with the morphologic observation of tuberculous cavities during the clinical course of pulmonary tuberculosis. A phase of the morbid process is seen which has been inaccessible to the eyes of the pathologist before the era of pulmonary resection, and the interpretation of which rested solely on the study of roentgenographic images.

Cavity Healing and Bronchial Occlusion:

The above cases, all of the post-primary type of tuberculosis, offer stimulating material for the study of cavity healing.

Group I presented active cavities, air-containing, with patent tuberculous bronchi.

Group II presented the beginning of cavity healing. The cavities were now round foci, with inspissated content. The draining bronchi were narrowed and could not be probed, though microscopically they presented some lumen. They showed active tuberculosis in their walls.

Group III presented a more advanced stage in cavity healing. Here, too, the cavities were round foci with inspissated content. The draining bronchi were grossly blocked, closed partly, or, in one instance (Figure 7c, Case 18), completely. The narrowing of these bronchi apparently took place in the scar tissue encircling the cavity. Beyond the scar, as the bronchi approached the hilar region, they were usually dilated and non-tuberculous. It is reasonable to assume that these bronchi once showed tuberculosis, which had cleared.

In 1942 Pagel and Simmonds[11] reviewed 33 instances of cavity healing, including 11 cases of their own. They concluded that the most common form of healing was the solid focus due to retention, inspissation, and calcification of contents. This impression, based on autopsy material, is confirmed by the surgical specimens described above. Pagel and Simmonds also felt that occlusion of the draining bronchi (either by obstructive caseous bronchitis, or by formation of a caseous plug) is largely instrumental in this form of cavity healing. This fact, too, tends to be confirmed by the surgical material, which, particularly in groups II and III, showed extensive tuberculosis of the draining bronchi with accumulation of abundant debris in the lumen. It is apparent, too, that one result of this bronchial tuberculous damage is healing with fibrosis and almost complete obliteration of the lumen.

Though, clinically, in most of the cases of groups II and III,

TABLE II

PATHOLOGICAL FINDINGS

Group	Case	Cavity	Bronchi Draining Cavity	Distant Bronchi*	Disseminated Tuberculosis	Hilar Bronchi
I	1	5 cm lining caseous	patent, tbc	no tbc	encaps cas foc prolif tbc foc	tbc
	2	4 cm lining caseous	patent, tbc	tbc	encaps cas foc	tbc
	3	2 cm lining caseous	patent, tbc	tbc	encaps cas foc prolif tbc foc	tbc
	4	2 cm lining caseous	patent, tbc	tbc	acute tbc pn	tbc
	5	2 cm lining caseous	patent, tbc	tbc	encaps cas foc	tbc
	6	2 cm lining caseous	patent, tbc	tbc	encaps cas foc fibrocas tbc	tbc
	7	3 cm part fill c̄ cas debris	patent, tbc	tbc	encaps cas foc	tbc
	8	2 cm part fill c̄ cas debris	patent, tbc	tbc	encaps cas foc	tbc
	9	2 cm part fill c̄ cas debris	patent, tbc	tbc	encaps cas foc	tbc

* Most of the cases that had no distant bronchial tuberculosis did have encapsulated caseous foci, some of which represented preceding caseous bronchitis.

TABLE II

PATHOLOGICAL FINDINGS (Continued)

Group	Case	Cavity	Bronchi Draining Cavity	Distant Bronchi*	Disseminated Tuberculosis	Hilar Bronchi
II	10	3 cm fill c̄ cas debris	one grossly pat, no tbc	no tbc	no tbc	no tbc
	11	1.5 cm fill c̄ cas debris	one grossly pat, tbc	no tbc	encaps cas foc	no tbc
	12	3 cm fill c̄ cas debris	grossly blocked, tbc	tbc	encaps cas foc prolif tbc foc	tbc
	13	2 cm fill c̄ cas debris	grossly blocked, tbc	tbc	encaps cas foc	tbc
	14	1.5 cm fill c̄ cas debris	grossly blocked, tbc	tbc	active cas foc	tbc
	15	3.5 cm fill c̄ cas debris	grossly blocked, tbc	no tbc	encaps cas foc	tbc
III	16	3.5 cm fill c̄ cas debris	grossly blocked, no tbc	no tbc	encaps cas foc	no tbc
	17	3 cm fill c̄ cas debris	grossly blocked, no tbc	no tbc	encaps cas foc	tbc
	18	3 cm fill c̄ cas debris	grossly blocked, no tbc	no tbc	encaps cas foc	no tbc
	19	1.5 cm fill c̄ cas debris	grossly blocked, no tbc	no tbc	encaps cas foc	no tbc
	20	2 cm fill c̄ cas-calcif debris	grossly blocked, no tbc	no tbc	encaps cas foc	no tbc
IV	21	scar (small central cas)	no tbc	no tbc	encaps cas foc prolif tbc foc	no tbc
	22	scar (small central cas)	no tbc	no tbc	prolif tbc foc	no tbc

some regression of the lesions were noted by x-ray preoperatively the cavities of both groups usually remained significant in size. This maintenance of size of the cavities lends anatomical support for the contention that cavity "healing" takes place by means of early blocking of cavity drainage.

Group IV presented two instances of cavity healing by scar formation. In both cases there was roentgenographic evidence of a preexisting cavity at the corresponding site. Both scars had evidence of small residual caseous centers. Pagel and Simmonds suggest that where the bronchus is more patent and the drainage more free, there is less material to form a large solid nodule; or where the closure of a cavity is a slower process, with a concentric shrinking of cavity wall, the final result is a scar. It is interesting to note that Case 21 was the only one of the series which had had a long-standing five-year thoracoplasty; the result of the slow cavity healing was a scar.

The Bronchi Draining the Cavity:

In group I, where the cavity drainage was grossly patent, all draining bronchi presented tuberculosis. The tuberculosis of these bronchi was most severe where they leave the cavity. Sections taken of these bronchi approaching the hilar region showed a definite diminution in the severity of the tuberculosis, though even

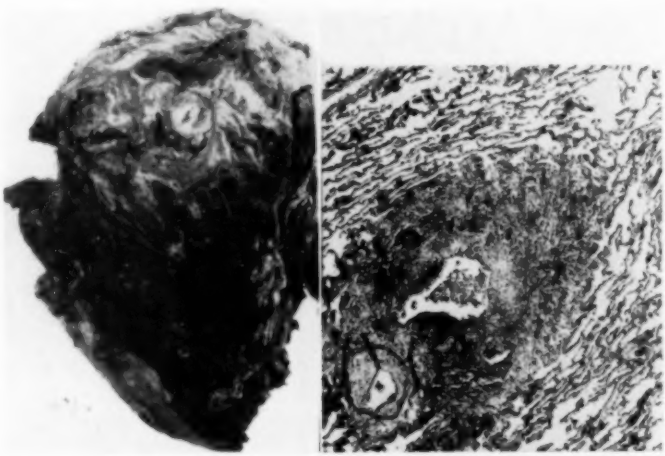

FIGURE 3a FIGURE 3b

Figure 3, Group I, Case 9: Resected apical segments of left upper lobe with large cavity partly filled with inspissated caseous debris. Patent tuberculous draining bronchi.—*Figure 3b, Group I, Case 9:* Tuberculosis of a distant bronchus, in lower part of specimen, Figure 3a.

in the hilar bronchial sections some tuberculosis of varying severity was still seen.

In group II, where cavity drainage was only beginning to shut down, the draining bronchi still showed extensive ulcerative, caseous and proliferative tuberculosis, and were sometimes plugged with caseous debris. Here, too, the severity of the tuberculosis of the bronchi diminished in intensity as the hilar region was approached. Sections of hilar bronchi showed considerable peribronchial fibrosis with the occasional proliferative tubercle, frequently submucosal.

In group III, where the narrowing or the plugging of the draining bronchi resulted in almost complete functional obliteration, there was, usually, no tuberculosis of the draining bronchi, and no tuberculosis of the hilar bronchi. The bronchial narrowing, by scarring, as these bronchi leave the cavity, probably occurs simultaneously and at the same increased tempo as the pericavitary fibrosis. Such complete healing of the draining bronchi, beyond their obstruction, is probably not entirely due to antibiotic therapy or individual resistance, but must in part be secondary to the elimination of the cavitary source of infection.

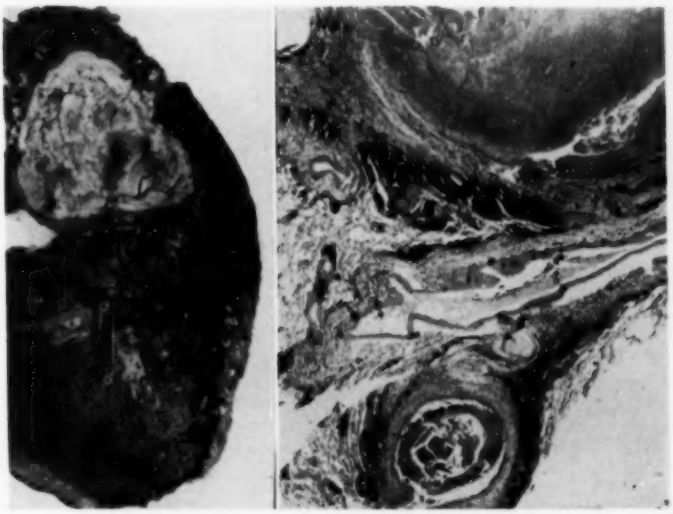

FIGURE 4a FIGURE 4b

Figure 4a, Group II, Case 12: Resected apical segment of left lower lobe with large cavity filled with inspissated caseous content. Draining bronchi grossly blocked.—*Figure 4b, Group II, Case 12:* Cavity with caseous content, and draining bronchus (below) plugged with caseous debris.

The above findings support the impression received from the study of autopsy material, that tuberculous bronchitis tends to be most severe in those bronchi which drain cavities, and that the mode of infection tends to be implantation of the tubercle bacilli.

Bronchi Running From the Cavity Towards the Overlying Pleura:

In the majority of the cases, with the healing of the cavity, there was tuberculous fibrosis of the parenchyma between cavity and pleura, with retraction of the overlying pleura. In two instances (Cases 10 and Case 18, Figure 7a), passages filled with caseous debris could be probed beyond the cavities. These passages probably represent tuberculous bronchiectasis. The plugging of the draining bronchi, with the conversion of the cavity into a solid focus appears to have resulted in retrograde bronchiectasis, such as is seen behind a solid tumor of the lung, this bronchiectasis becoming tuberculous. The pathogenesis could also be that of initial tuberculous infection with resultant bronchial destruction. The finding of these retrograde caseous projections points to a possible mechanism of spread of a cavity and also raises the question whether the cavity itself may have started in a bronchus. This would be difficult to prove. The area of lung parenchyma involved by the cavity, at the time the specimen is viewed, is too

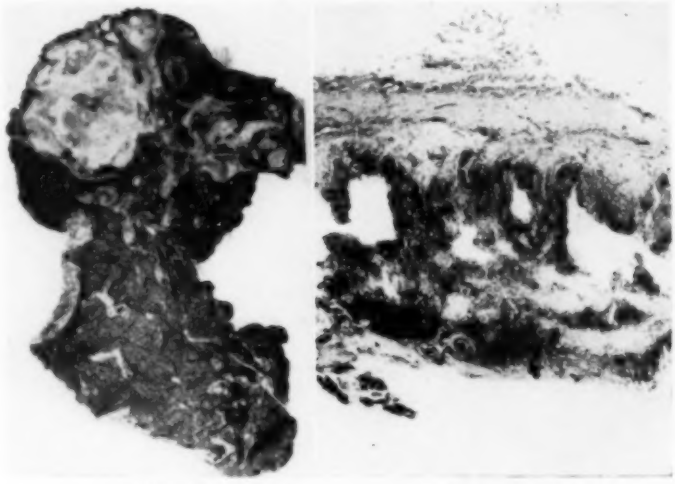

FIGURE 5a FIGURE 5b

Figure 5a, Group II, Case 15: Resected apical segments of left upper lobe, with large cavity filled with inspissated caseous debris. Draining bronchi grossly blocked.—*Figure 5b, Group II, Case 15:* Grossly blocked draining bronchus narrowed by wide layer of tuberculous granulation tissue.

large to permit speculation as to the pathogenesis of its mode of origin.

The Distant Bronchi:

Bronchi some distance removed from the cavity were sectioned routinely. In group I, where the cavity was open, the bronchi patent and tuberculous, the majority of the cases showed some tuberculosis of the distant bronchi.

In group III, where the cavity content was inspissated, and the drainage negligible, the distant bronchi showed no tuberculosis, though some of the distant encapsulated foci undoubtedly represent a previous tuberculous bronchitis.

It would therefore seem reasonable to conclude that tuberculosis, not only of the bronchi draining the cavities, but of the distant bronchi as well, is, in the majority of cases, dependent on the existance of a cavity, and that the mode of infection is probably by implantation.

Not one of the 22 cases was an example of tuberculous bronchitis without the presence of a cavity.

The Foci of Tuberculous Dissemination:

Each surgical specimen, in addition to the evidence of the existance of a cavity, presented some form of tuberculous dissemination.

The presence of a diffuse tuberculous bronchitis has already been pointed out in those cases with draining cavities.

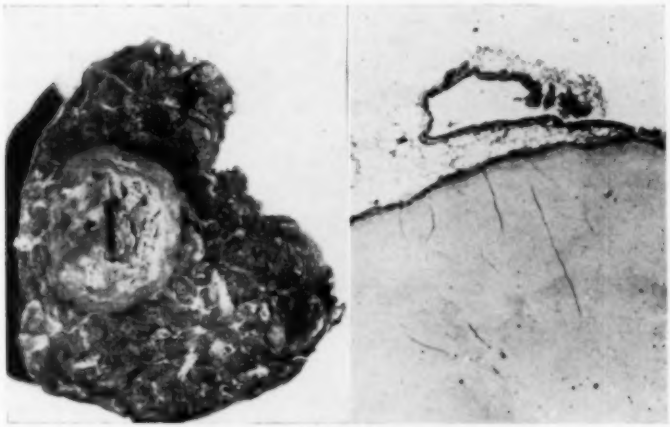

FIGURE 6a FIGURE 6b

Figure 6a, Group III, Case 16: Resected left upper lobe with large cavity filled with caseous debris. Draining bronchi grossly blocked.—*Figure 6b, Group III, Case 16:* Cavity wall, wide layer of hyalinized fibrous tissue encloses the caseous content. Clean draining bronchus, apparently beyond its block.

FIGURE 7a

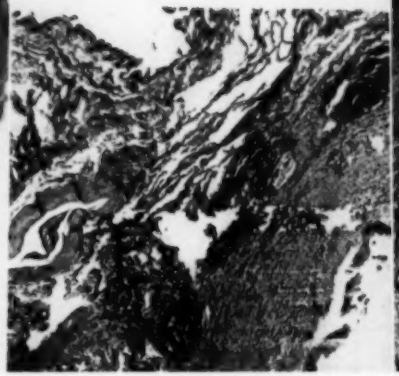

FIGURE 7b

FIGURE 7c

Figure 7a, Group III, Case 18: Resected segments of left upper lobe and left lower lobe. Lower half of specimen shows cavity filled with inspissated caseous content; above the cavity there is retrograde communication with elongated caseous foci running to pleura, apparently caseous bronchiectasis.—*Figure 7b, Group III, Case 18:* Clean draining bronchus, apparently beyond block, in upper left corner. Cavity wall, with caseous content, in lower opposite corner.—*Figure 7c, Group III, Case 18:* Draining bronchus occluded by fibrosis, within dependent region of wall of cavity seen in Figure 7a.

Almost every specimen, in all four groups, has encapsulated caseous foci. Microscopy, including occasional staining for elastic tissue, showed that many of these caseous foci involved a bronchiole and surrounding alveoli, representing the delimitation of an area of caseous bronchopneumonia. A number of these encapsulated caseous foci appeared to have been, originally, a tuberculous bronchus filled with caseous debris, now encapsulated, the bronchus itself obscured. If one were to judge from the histological pattern alone, one would conclude that most of the encapsulated caseous foci are of the bronchogenic dissemination type.

In many of the specimens of all groups, old fibrosis, small patches of proliferative tuberculosis, and bronchopneumonic patches of proliferative tuberculosis with central caseation, were seen. Few of the cases showed evidence of acute exudative or early caseous pneumonia.

The existance of disseminated tuberculosis throughout the resected specimen points to the fact that such foci also exist within the lung tissue left behind.

The Plane of Resection:

The hilar plane of resection ran through the lobar bronchus in lobectomies, and through bronchi of a smaller order in segmental resections. Evidence of tuberculosis of these hilar bronchi was found in almost all of the cases that had tuberculosis of the draining bronchi. However, the infection usually presented itself in the form of an occasional subepithelial tubercle.

In segmental resections, the plane of surgery took place through tuberculous tissue in most of the cases. Usually the tuberculosis was in the form of quiescent encapsulated foci with central caseation, or indolent proliferative nodules. At times the resection ran through caseous bronchitis or occasionally broke into a cavity. Tuberculous postoperative complications were infrequent.

The Role of Streptomycin:

Streptomycin was used preoperatively in all the cases. The object was to intervene surgically in the midst of a course of therapy. While there are no gross or histological criteria that can be attributed to streptomycin alone, it is felt that the drug may have increased the tempo of healing. Early inhibition of the multiplication of the tubercle bacilli may lead to early inspissation of cavity contents, and early plugging of draining bronchi. Streptomycin may hasten the healing of the tuberculous bronchitis of the draining bronchi and thus may precipitate the fibrotic narrowing of the bronchi as they leave the cavity, with resultant early blocking of the bronchi. The drug may thus increase the tendency for the formation of round foci which are apt to be large, and a

potential source of danger. It would seem, therefore, that an important place for the use of streptomycin is as a preoperative measure to be followed by resection. Streptomycin was also used through the postoperative period and many months afterwards, and probably played its part in preventing both immediate postoperative tuberculous spread and late exacerbations by keeping the bacillary population low and nonvirulent.

The Influence of Collapse Therapy on the Pathology Seen:

Pagel and Simmonds[11] tend to attribute early closure of draining bronchi to the superposition of pneumothorax therapy on bronchi already partially obstructed by caseous bronchitis. All of the cases of group III had no previous collapse therapy (except for Case 18, in which there was a pre-resection "tailoring" thoracoplasty of four weeks duration). One can conclude there, that collapse therapy is not necessary for early closure of draining bronchi.

SUMMARY

Surgically removed anatomical units of lung tissue in pulmonary tuberculosis are becoming more abundant. This material, investigated with careful clinical-pathological correlation, will offer a great deal of information concerning the pathogenesis of the disease.

Twenty-two specimens representing lobectomies and segmental resections for pulmonary tuberculosis were reviewed. The pathology of the cavity, its stage of healing, and related tuberculous processes in each specimen, were studied. Salient points that can be deduced are:

1) Cavity "healing" takes place most frequently by the formation of a round focus, with blockage of the draining bronchi.

2) The round focus tends to be large, in part due to the rapid tempo of cavity healing enhanced by streptomycin.

3) This round foci, the most frequent "healed" variant of the tuberculous cavity, is potentially dangerous, and can readily reactivate.

RESUMEN

Las unidades anatómicas con tuberculosis pulmonar extraídas quirúrgicamente, van siendo más abundantes. Este material investigado con una correlación clínica y patológica cuidadosa, irá proporcionando una valiosa información sobre la patogenia de la enfermedad.

Se han revisado 22 especímenes de lobectomías y resecciones segmentarias. La anatomía patológica de la caverna, su estadio de curación y los procesos relativos tuberculosos en cada especimen fueron estudiados. Los puntos salientes que se pueden deducir son los siguientes:

1) La "curación" de la caverna se verifica lo más frecuentemente por la formación de un foco redondo con bloqueo del bronquio de avenamiento.

2) El foco redondo tiende a ser grande en parte debido a la rapidez de la curación de la cavidad acentuada por la estreptomicina.

3) Este foco redondo, la variante más frecuente de la caverna tuberculosa "curada" es potencialmente peligroso y puede reacticarse fácilmente.

RESUME

Les pièces anatomiques de tissu pulmonaire qui ont été l'objet d'une exérèse chirurgicale deviennent plus abondantes. Ce matériel, étudié avec soin à la fois anatomiquement et cliniquement offrira des informations importantes au sujet de la pathogénie de l'affection.

Vingt-deux pièces provenant de lobectomies ou de résections segmentaires pour tuberculose pulmonaire ont été étudiées par les auteurs. Ils ont étudié l'anatomie des cavernes, leur stade de guérison ainsi que l'ensemble des lésions tuberculeuses. Ils ont pu en déduire quelques points importants:

1) La guérison des cavernes se fait le plus fréquemment par la constitution d'un foyer rond avec blocage de la bronche de drainage.

2) Ce foyer rond, qui est la façon la plus habituelle de guérir pour la caverne tuberculeuse comporte un potentiel évolutif dangereux et peut subir una réactivation.

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Chest Surveys of the Aged

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Few reports appear in the literature concerning tuberculosis case finding in "Old Folks" homes. Myers[4] calls attention to the reservoir of contagious tuberculosis in the aged. Mediar[2,3] reported an increasing incidence of tuberculosis in the "over 50 year" group that came to autopsy during 1940-1945 as compared to a similar group autopsied in 1916-1920 in New York City.

In 1942, in 1945 and again in 1949, The Baltimore City Hospitals, Baltimore, Maryland, has held mass chest surveys of its Infirmary patients. The purpose of this paper is to present information gained from these surveys as they offer material that would probably be characteristic of data obtained through a survey of any public home for the elderly.

Material and Methods

In the 1942 survey 670 persons had 35 mm. film inspections of their chests. All films were interpreted by a physician from the United States Public Health Service National Institute of Health, Division of Tuberculosis. In 1945 the survey was repeated. This time 636 persons were photofluorographed on 70 mm. film. All films were interpreted by a phthisiologist. In 1949, 581 inmates of the same group were surveyed on 70 mm. film, but this time the films were interpreted by a radiologist. The findings are summarized and compared in Table I.

There have been several recent papers illustrating variations in the interpretations of survey films depending on the ability, experience and degree of fatigue of the reader. The present report is also of interest because the same group of patients was surveyed three times, the films of each survey being read by a different type of specialist. The films of the first survey were read by an epidemiologist whose basic outlook was that of a clinician in the research field. The films of the second survey were read by a specialist in chest diseases who was interested primarily in tuberculosis, and who had probably had more experience with that disease than either of the two other readers. The films of the third survey were read by a radiologist who was not influenced from

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Table I: Note "over-reading" of films by clinician, "under-reading" of films by phthisiologist and "mean-between-the-two" by radiologist.

	1942 U.S.P.H.S. M.D.	1945 Phthisiologist	1949 Radiologist	1942 U.S.P.H.S. M.D.	1945 Phthisiologist	1949 Radiologist
	Number of Cases			Percentages		
Total No. Chests Examined	670	636	581			
Healthy Chests	476	554	469	71.1	87.1	80.7
Tuberculosis	88	49	85	13.1	7.7	14.6
Abnormalities of Heart and Aorta	24	25	14	3.6	3.9	2.4
Other Diseases	82	8	13	12.2	1.2	2.2

Table II: Showing break-down and comparison of findings noted in positive cases in all three surveys.

	1942 U.S.P.H.S. M.D.	1945 Phthisiologist	1949 Radiologist	1942 U.S.P.H.S. M.D.	1945 Phthisiologist	1949 Radiologist
	Number of Cases			Percentages		
Total Chests Examined	670	636	581			
Total No. Cases Thought to be Tuberculosis	88	49	85	13.0	7.7	14.6
Minimal Tuberculosis	22	16	38	3.2	2.5	6.5
Moderately Advanced	18	17	24	2.7	2.7	4.1
Far Advanced	2	3	5	0.3	0.5	0.8
Suspicious Lesion	46	13	18	6.8	2.0	3.1

either the clinical standpoint or from the phthisiologist's viewpoint, but who initiated the survey with two objectives in mind: (1) To find active tuberculosis. (2) To compare the results of his survey with the others that had been performed previously. This description of the readers is given because many intangible factors are thus brought into the picture.

It is interesting to note that the results show the epidemiologist "over-read" the films (71 per cent negative), the phthisiologist "under-read" the films (87 per cent negative) and the radiologist hit a middle path (80.7 per cent negative). Apparently the phthisiologist's more varied experience with tuberculosis enabled him to consider inactive or insignificant many lesions which the other two readers considered positive. The clinician found a significant percentage of other diseases (12.2 per cent cardiac enlargement, etc.) which the phthisiologist tended to ignore. However, again the radiologist took the "middle path" averaging 2.2 per cent positive cases.

Those cases showing any type of inflammatory change in the lungs, regardless of apparent age of the lesion, were listed as being suspicious for tuberculosis of undetermined activity. They were further subdivided into four groups. Table II illustrates the breakdown of these findings.

Cases having positive findings in the 1949 survey were referred to the medical service of the general hospital for careful study. Many had been seen there previously and already had undergone sufficient study to establish a final diagnosis.

Table III: Final classification of cases of 1949 survey after extensive clinical, laboratory and radiological follow-up.

		Per cent of 85 Positive Cases	Per cent of Total Survey Cases (581 cases)
Fibroid Infiltration	49	57.7	8.4
Minimal	28		
Mod. Adv.	16		
Far Adv.	5*		
Fibrocalcific Changes	9	10.5	1.5
Minimal	8		
Mod. Adv.	1		
Exudative Lesions	9	10.5	1.5
Minimal	2		
Mod. Adv.	7**		
Other Diseases	18	21.2	3.0

*1 active case of pulmonary tuberculosis in this group.
**2 active cases of pulmonary tuberculosis in this group.
0.5 per cent of 581 cases had active tuberculosis.

There were six patients known to have had active pulmonary tuberculosis at one time, but who had eventually been considered as arrested cases. Of these, two had undergone thoracoplasties and a third one had been re-admitted to the tuberculosis division as an active case. There remained 79 patients with chest lesions suspicious for pulmonary tuberculosis. All of these cases had serial 14 x 17 inch films repeated at six week intervals until activity was noted or until the lesion was considered static. History, physical examination and sputum studies were carried out in all but 17 cases. It was not possible to obtain sputa or gastric cultures on these cases because of their age, mental and physical conditions.

Results

Of this entire group only three had positive cultures. Following complete evaluation over a 10 month period on the total group of 85 patients who had roentgen evidence of some type of pulmonary lesion in the initial survey, 64 were classified as having inactive tuberculosis. The remaining 18 had other diseases such as bronchiectasis, massive pleural calcifications and pneumonia. (See Table III).

It is worth noting that retakes in surveys of the aged are considerably higher than in surveys of a general population. In the above surveys approximately 20 per cent of the patients were re-examined on 14 x 17 inch films as compared to the usual 3 or

Table IV: Table shows marked increase in number of retakes required in examining old people on survey equipment. It also demonstrates the high percentages of lesions that must be regarded with suspicion necessitating long follow-up studies. In spite of such high percentages only 0.5 per cent of the cases in the survey showed active disease.

	Population Hagerstown, Md.* 1948-49	Pct.	Baltimore City Hospitals Infirmary Baltimore, Md 1949	Pct.
Total People Examined	18,856		581	
Total Retakes Requested	668	(3.5)	119	(20.5)
Total Negative Retakes	463	(2.4)	7	(1.2)
Total Cases Tuberculosis	123	(0.6)	67	(11.5)
Minimal	90	(1.47)	38	(6.5)
Mod. Adv.	27	(0.14)	24	(4.1)
Far Adv.	6	(0.03)	5	(0.86)
TOTAL	123		TOTAL 67	
Total Cases Other Diseases	47	(0.2)	45	(7.7)

*Figures obtained through courtesy of Dr. P. S. Lawrence, Biostatistician, U.S.P.H.S.

4 per cent re-examined in general surveys. Reasons for this may be classified as follows:

A) Technical Difficulties:
   1) Involuntary motion — Parkinsonism, deafness, weakness, "crankiness".
   2) Positioning — Kyphosis, arthritis and other bony deformities.
   3) Artifacts — patients conceal personal belongings under clothes.
   4) Clerical—maintenance of order and line-up; patients give wrong names or forget their names; incontinence causes frequent leaving of line.

B) Increased incidence of residue of diseases of earlier life—scars and fibrosis from pulmonary infections earlier in life are common.

It is of interest to compare this survey of an aged group with one of an average population of all ages (Table IV).

Discussion

The few articles which have appeared in the literature lead one to feel that a high incidence of active pulmonary tuberculosis might be found in a mass chest survey of an infirmary for the aged. One would think this to be especially likely in a public institution where all of the patients are indigent cases. The exact opposite proved to be the case. There was low incidence of active disease. The explanation probably lies in the fact that admission to the infirmary of this particular hospital is preceded by a screening physical examination at the Department of Welfare. A more careful history and a physical examination are then performed in the general hospital through which the patient is admitted to the home for the aged. In recent months, since the 1949 survey began, a routine admission chest x-ray film has become an established procedure.

SUMMARY

1) Mass surveys of elderly persons in a home for the aged are difficult to carry out.

2) The incidence of old, inactive pulmonary disease is high.

3) Quite the opposite of other reports in the literature was discovered. The incidence of active pulmonary tuberculosis in the aged is very low in this group probably because of the careful screening admission examination. In this study only three active cases of tuberculosis were discovered and one of them was a known case already under observation.

4) The incidence of diseases, other than tuberculosis, is high. Especially common were lesions of the cardiovascular system.

RESUMEN

1) Un trabajo en masa sobre la salud de los ancianos en asilos para ellos, es difícil.

2) La incidencia de tuberculosis antigua inactiva es alta.

3) Muy diferente en lo encontrado en otras publicaciones fué lo que se descubrió. La incidencia de tuberculosis pulmonar activa es muy baja en este grupo, probablemente debido a la cuidadosa selección para la admisión. En este estudio solo se encontraron tres casos de tuberculosis y uno de ellos era un caso ya conocido bajo observación.

4) La incidencia de otras enfermedades aparte de la tuberculosis es alta. Especialmente son comunes las lesiones cardiovasculares.

RESUME

1) Les examens systématiques des personnes âgées placées dans les établissements de vieillards sont très difficiles à mener à bien.

2) La fréquence de la tuberculose ancienne et inactive est très élevée.

3) Les auteurs ont fait des constatations tout à fait opposées à celles qui peuvent être relevées dans la littérature. La fréquence de la tuberculose pulmonaire active est très basse dans le groupe qui à été examiné. Ceci tient sans doute au soin avec lequel l'examen systématique est fait lors de l'er.'·ée. Dans cette étude, on ne put mettre en évidence que trois cas de tuberculose active, et l'un d'entre eux était déjà connu auparavant et mis en observation.

4) La fréquence d'autres affections que la tuberculose est élevée. Les lésions de l'appareil cardio-vasculaire en particulier sont nombreuses.

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Arteriovenous Fistula of the Lung and an Associated Hemangioma of the Vertebra: Case Report

JAMES W. NIXON, M.D., F.C.C.P. and
JOHN F. PERRY, M.D.
San Antonio, Texas

The subject of arteriovenous fistulae is of interest not only because such lesions are of unusual occurrence, but also because these cases are amenable to surgical treatment, with satisfactory results being expected therefrom. It is likewise interesting that the description and the diagnosis of this disease have been recorded only since modern thoracic surgery has been able to offer relief.

In the earliest reports, Reading in 1932,[11] and later Rodes in 1938,[12] presented each a case. Both of these cases had shown manifestations of polycythemia, clubbing, and cyanosis though neither case had been diagnosed during life. At autopsy both cases had been shown to have a pulmonary hemangioma or arteriovenous fistula. The literature of the decade following the latter report is found to contain more numerous examples of the disease, manifested by the same group of symptoms. A most recent and most excellent review of the literature is given by Yater, et al.,[13] in which 45 cases are presented.

Pulmonary arteriovenous fistula is a disease belonging to the class of hereditary hemorrhagic telangiectasia and it is possible to demonstrate cutaneous and mucous membrane lesions in 50 per cent of those afflicted.[2]

The etiology is not known beyond the fact that the lesion is congenital and that the tendency is apparenly familial, since pulmonary lesions, as well as generalized telangiectasia have been found in siblings and parents of patients with pulmonary arteriovenous fistulae. The tendency is apparently transmitted as a simple dominant characteristic, with both sexes being affected.

The onset of symptoms may occur at ages ranging from birth to the third decade. The congenital character of the disease and the late onset of symptoms suggest that the lesions are progressive. Once the vascular channels of pulmonary hemangioma have become enlarged to the point of functioning as an arteriovenous fistula in the lesser circulation, a characteristic symptom complex appears: The patient, usually in the third or fourth decade of life, becomes cyanotic although the heart is normal in both size and

function. Dyspnea, hemoptysis, transient dizziness and cerebral manifestations of numbness and paresthesias may occur. There is clubbing of the digits, and the presence of telangiectasia may be found throughout the skin and mucous membranes. Both the blood-pressure and the pulse remain normal and no enlargement of the spleen occurs. Over the lung fields there may be an audible bruit.

Laboratory examinations reveal the presence of polycythemia, with increased red blood cells, hemoglobin, and hematocrit. The white blood count remains normal. Arterial oxygen saturation is reduced. This reduction, it has been found, is inversely proportional to the degree of polycythemia present, which condition in turn reflects the degree of arteriovenous shunting that is occurring in the pulmonary arteriovenous fistula.[10]

X-ray examination of the chest demonstrates one or more circumscribed lobulated densities in the lung field which may pulsate fluoroscopically. Laminograms and angiography may demonstrate tortuous vessels leading from the hilus to the area of increased density. The heart shadow is normal in size. Coupled with the clinical picture the x-ray findings may be considered practically diagnostic.

The prognosis in untreated cases and in cases unsuitable for radical treatment is poor. The major threats of thrombosis resulting from increasing density of the blood, or of pulmonary hemorrhage by rupture of the lesion into a bronchus, are the chief indications for surgery; but symptoms secondary to polycythemia must be included in the criteria.

In the differential diagnosis of this disease, the following possible conditions must be considered: (1) polycythemia vera, (2) secondary polycythemia, which may be due to (a) high altitude, (b) poisoning from heavy metals or amaline dyes, (c) pulmonary diseases such as Ayerza's Disease or emphysema, both of which prevent adequate oxygenation; and (d) cardiac anomalies with a right-to-left shunt.[9]

In the roentgen diagnosis of the lesion, cysts, adenomas, metastatic lesions, tuberculoma, and aneurysm of pulmonary artery branches must be ruled out. Pulmonary densities must not be confused with those that are secondary to infarcts in cases of polycythemia vera.

A peripheral arteriovenous shunt increases all elements of blood volume proportionally and likewise increases cardiac output with an accompanying dilatation of the heart. A pulmonary shunt has little effect on either cardiac output or cardiac dynamics.[8] The increase in red cell mass is secondary to decreased oxygenation

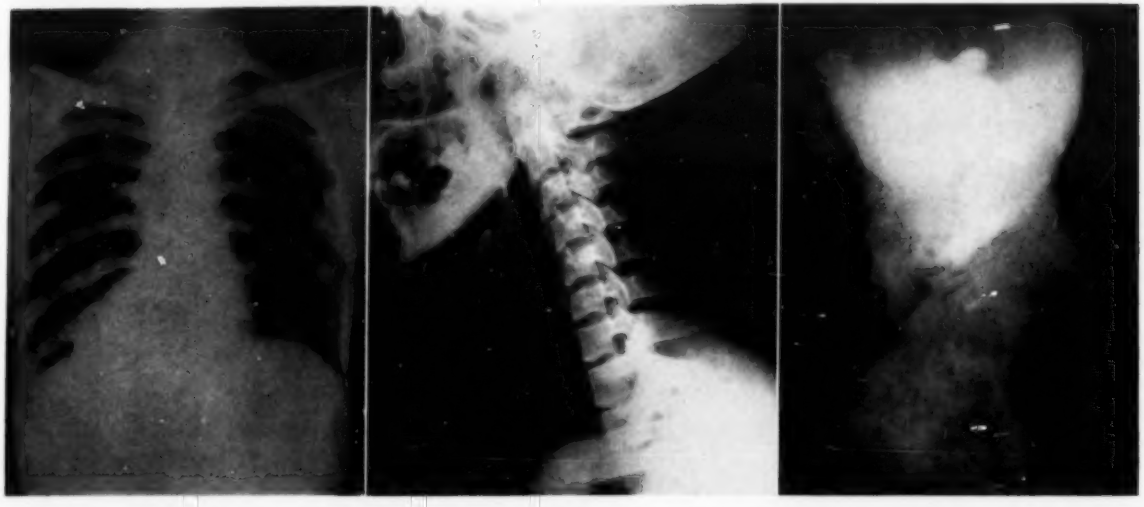

FIGURE 1 FIGURE 2 FIGURE 3

Figure 1: A-P projection of chest showing anterior-venous aneurism in left lower lung field. The enlarged pulmonary hilar vessels are evident.—*Figure 2:* Lateral view of cervical spine showing hemangioma of third cervical vertebra.—*Figure 3:* X-ray film of barium filled surgical specimen showing extent of arterio-venous aneurism.

of the blood in the pulmonary circuit. The blood-pressure remains normal, the heart does not enlarge.

Moyer and Ackerman,[10] in reviewing the pathology of several pulmonary arteriovenous fistulae, found these lesions to consist of distended afferent arteries and distended efferent veins. The intercommunicating capillaries which normally function between the arteries and the veins were absent and in their place was found either large vascular trunks furnishing direct communication or else a mass of distended vessels. Degenerative changes had occurred in the vessel walls due to arterial pressures having been transmitted directly to the abnormal vessels and veins.

The treatment of pulmonary arteriovenous fistulae is surgical. Hepburn and Dauphinee[6] in 1942 reported the first cure by pneumonectomy. Yater, et al.,[13] series includes 26 operated cases, two of which died post-operatively. The choice of pneumonectomy, single or multiple lobectomy, or segmental resection will depend upon the number, extent, and distribution of the lesions.

The following case report is presented because the relative infrequency of this lesion warrants description of individual cases and because we believe that this specific example presents certain features which have not hitherto been described.

Case Report

M. H., a 26 year old Latin-American male was admitted to the Santa Rosa Clinical Service November 8, 1949, with a chief complaint of pain in the neck and dyspnea on exertion. The neck pain had developed seven months prior to his admission, in the right posterior auricular region, and had increased in severity somewhat with radiation to the right posterior triangle of the neck. The pain was severe enough that he had stopped working at its onset. There was no history of trauma. The second complaint of dyspnea, coupled with easy fatigability, had been present since age eight. At this time a school physician had noted that the boy's fingernails were blue and enlarged. A diagnosis of "heart trouble" had been made at this time and he was advised to refrain from strenuous activity. He completed the sixth grade in school and had since worked in a cleaning and pressing shop until onset of his neck pain in April 1949. He had been known in his community as the "Blue Boy." Past history was negative except for one attack of pneumonia during childhood. Family history was significant in that a paternal aunt had had a similar affliction.

Physical Examination demonstrated a tall, thin male of about stated age, cyanotic, with no respiratory distress. Cyanosis was particularly noted in the nail beds, lips, tongue, and face. There was marked tenderness in the right post auricular area and tenderness of the musculature of the neck below the right mastoid. Discrete, shotty, lymph nodes were palpable bilaterally, with one larger node on the right. There was increased pain on turning the head, referred to the right post auricular area. The teeth were carious with marked pyorrhea. The tongue was dark red in color. A deformity of left third, fourth, and fifth ribs consisting

of slight elevation was present. The heart was not enlarged and heart sounds were normal. Expansion was equal bilaterally and the breath sounds were normal. Over the left posterior chest there was heard a bruit, unrelated to the cardiac sounds. The remainder of the physical examination was negative except for cyanosis and marked clubbing of the digits. Blood-pressure was normal.

Laboratory Examinations: RBC 9,280,000; HBG 137 per cent, 21 gms.; WBC 7,500 with normal differential; MCV 72 cu. microns; MCH 23 micromicrograms; M CHC 31 per cent; Hematocrit 66 per cent. Circulation Time (3 cc. Decholin) 34 Sec. Vital Capacity 62 per cent of normal or 2.9 litres. Urine negative. Stool negative for occult blood. Serum acid phosphatase 5 units.

X-ray examination of the chest demonstrated a smooth, rounded, soft tissue mass six cm. in diameter in the left lower lobe with many markedly dilated vessels extending from this mass to the hilus. No definite pulsation of the mass was seen but there was some pulsation of the vessels extending from the hilus. The heart was slightly enlarged, predominantly left ventricular. A roentgen diagnosis of pulmonary arteriovenous aneurysm was made. X-ray films of the cervical spine demonstrated loss of normal lordosis and demineralization with irregular mottled osteoporosis of C_3 suspicious of neoplastic destruction.

Electrocardiograms were reported basically normal with a single nodal extra systole.

In view of the elevated acid phosphatase, and of the evidence of destruction of the third cervical vertebra, diagnosis of neoplastic destruction of third cervical vertebra and the presence of an arteriovenous fistula of the lung was made.

The patient received ten x-ray treatments of 165 R each to the cervical spine with marked improvement. He was discharged November 26, 1949, to be followed in the cardiac clinic in order that the course of the cervical

FIGURE 4

FIGURE 5

Figure 4: Hand showing marked pulmonary osteoarthropathy.
Figure 5: Surgical specimen: The arteriovenous fistula is easily seen.

lesion might be determined following the x-ray therapy. He was re-admitted on January 5, 1950, with interval note that he had gained six pounds weight and that the pain in his neck was much improved. Repeat examination of cervical spine revealed no essential change. I. V. Pyelograms and x-ray of remainder of spine was negative. It was felt that since no primary site for neoplasm had been demonstrated, and that since the lesion of C_3 was apparently stable, that this probably presented a hemangioma of the vertebrae. Accordingly, the patient was seen by the senior author in consultation, and exploration of the left chest was decided upon. On January 19, 1950, operation was scheduled but was abandoned because bleeding from the gums was so marked following intubation for anesthesia that it was felt any surgery would be precarious.

After removal of several loose teeth, the patient was successfully anesthetized on January 28, 1950. The left chest was opened by subperiosteal resection of the sixth rib. Upon entering the chest the left lung was found to be densely adherent to the parietal pleura over a greater part of its surface. After freeing the lung it was found that the left pulmonary artery and left inferior pulmonary vein were dilated to three or four times normal size. A dark red globular mass occupied the greater part of the lower left lung. Over this mass a thrill was palpable which disappeared when the pulmonary artery was clamped, then reappeared with release of the artery. A total pneumonectomy was carried out with individual ligation of the great vessels with heavy braided silk and by closure of the bronchus with medium cotton. The hilus was repleuralized, and the chest was closed without drainage. Within a few seconds, following ligation of the pulmonary artery, the patient lost his cyanotic hue, became pink and has remained so.

During his post-operative course he was visited by many of his friends who came to see if the rumor were really true that he was normally pink and no longer the "Blue Boy." His post-operative course was satisfactory, without incident, and he was discharged on February 10, 1950. He was re-admitted March 4, 1950 with interval history that following his discharge from the hospital he had developed a cough which was particularly worse during eating and as a result of which he at poorly, lost weight and became malnourished. Fluroscopy with barium swallow failed to reveal any pathology. He was re-admitted because of cough and progressive weakness from malnutrition. On the afternoon of admission he developed 100.4 degrees F. temperature. The right chest was clear at this time, but by the following day the right chest was full of rales, with temperature of 102 degrees F., pulse 100 to 140, and with x-ray film revealing mottled congestion of right lung field. Cyanosis and dyspnea again developed. On this occasion the diagnosis of broncho-pneumonia was made. The patient responded to digitalis, antibiotics, and oxygen, and was discharged on April 8, 1950, recovered. His subsequent progress has been satisfactory.

Pathological Report: This lung weighs 450 gms. which is within the normal weight range. Externally the lung is pink in color and even in contour. Over the lateral surface of the superior lobe there are a few moderately dense adhesions. Otherwise the outer surface of the lung is smooth. On the medial aspect over the central portion of the lower lobe there is a swelling approximately 5 cm. in diameter and raised approximately 3 cm. above the surrounding lung. This represents the area over the aneurysm.

On cut section through the junction of the inferior pulmonary artery and vein a direct communication between the artery and vein is demonstrated. This was demonstrated before cutting into the lung by injection of a paraffin solution into the artery. The artery and vein each are approximately 3.0 cm. in diameter and the communication between the artery and vein is approximately 2.0 cm. in diameter. Diagnosis: Arteriovenous aneurysm between the inferior pulmonary artery and the inferior pulmonary vein.

Discussion

The explanation of the extreme degree of cyanosis which exists in these cases is that the resistance offered by the arteriovenous aneurysm is less than that offered by the capillaries of the normal lung. This results in a greater blood flow through the arteriovenous aneurysm than through the normal pulmonary capillary bed, as a result of which a larger volume of blood from the right ventricle passes through the pulmonary circuit and into the systemic circulation without being oxygenated.

Hemangioma of vertebra is an uncommon clinical finding although these lesions have been demonstrated in 10 per cent of routine autopsies by Schmorl (quoted by Ghormley and Adson[5]). These are usually asymptomatic and not demonstrable roentgenologically. A classification of these lesions by Foster and Heublein[4] is given below:

1) Asymptomatic discovered incidentally.
2) Symptomatic with localized radicular or spinal pain without objective signs of damage to nerve roots or spinal cord.
3) Hemangioma with subjective and objective signs or myelopathy.
4) Hemangioma which has undergone pathologic fracture and loss of normal contour of vertebral body with or without myelopathy.

Women are affected more often than men.[1] The commonest site for symptomatic lesions is the middle dorsal vertebrae. Bucy and Capp[1] reported no cases of cervical vertebral involvement being found.

Pathologically the intratrabecular areas are filled with dilated cavernous spaces instead of normal myelogenous tissue. These spaces are lined with a single layer of endothelial cells which rest on a thin network of connective tissue. Some trabeculae are seen lined with osteoblasts in process of new bone formation. Elsewhere erosion of bony spicules is evident.

The x-ray appearance of these lesions is characteristic.[7,3,1,5] The irregular absorption of bony trabeculae of the vertebral body and the thickening of the remaining trabeculae cause the appearance of coarse vertical and parallel striation in a field of decreased

density. The abnormal trabeculations may extend into the vertebral arches and laminae.

In the differential diagnosis of vertebral hemangioma, metastatic lesions of vertebral bodies are considered. In the presence of involvement of the spinal cord, intraspinal tumors are to be differentiated. Usually metastases produce symptoms more rapidly progressive than those produced by hemangioma. The primary malignant site can usually be demonstrated.

Most authors agree[4,7,3,1] that if the diagnosis can be made with any degree of certainty, deep x-ray therapy is the choice of treatment. Regression of symptoms occurs following roentgen therapy, but the appearance of the vertebral body does not change.

SUMMARY

In reviewing the cases of pulmonary arteriovenous fistulae that have been reported we have been unable to find a record of any such combination of lesions as that here described. Apparently the vertebral hemangioma represents but another manifestation of a generalized telangiectatic tendency in this patient. The response of the lesion to x-ray therapy, without demonstrable change in the appearance of the vertebral body, and the absence of any primary site from which a vertebral metastasis might arise, support the diagnosis of cervical vertebral hemangioma.

RESUMEN

Revisando la literatura sobre fístulas pulmonares arteriovenosas no hemos encontrado referido caso alguno de una combinación como la descrita aquí.

Aparentemente el hemangioma vertebral representa otra manifestación de la tendencia telangiectásica en este enfermo.

La respuesta de la lesión a la terapia sin cambio demostrable en la apariencia del cuerpo vertebral y la ausencia de cualquiera ubicación primaria de la cual pudiera haber emergido la metastasis vertebral, sostiene el diagnóstico de hemangioma de una vértebra cervical.

RESUME

En passant en revue les cas d'anévrysmes artérioveineux, les auteurs n'ont pu retrouvé l'association qu'ils décrivent ici. Apparemment, l'hémangiome vertébral ne représente qu'une autre manifestation de la tendance généralisée à la télangiectasie. La réponse favorable à la radiothérapie sans modification de l'aspect de la vertèbre, et l'absence de foyer primitif susceptible d'être à l'origine d'une métastase vertébrale, justifient le diagnostic d'hemangiome vertébral.

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NEW YORK POSTGRADUATE COURSE

The Fourth Annual Postgraduate Course on Diseases of the Chest, sponsored by the Council on Postgraduate Medical Education and the New York State Chapter of the College, was presented at the Hotel New Yorker, New York City, November 12-17, 1951. The course was attended by 138 physicians representing twenty-five states, the District of Columbia, Puerto Rico, Argentina, Brazil, Canada, Ceylon, Chile, France, Indonesia, Japan, Mexico and Spain. Canada with twenty-three physicians registered had the largest delegation outside of the United States.

A cocktail party sponsored by Armour Laboratories was held at the Hotel New Yorker on Monday, November 12, and a closing cocktail party was given on Friday night, November 16, by Smith, Kline and French.

The officials for this postgraduate course were: Dr. Edgar Mayer, Chairman, Dr. Frank R. Ferlaino, Co-Chairman, and Dr. Alfred S. Dooneief, Secretary. Dr. Emil A. Naclerio was in charge of the arrangements for the scientific assembly. Dr. J. Winthrop Peabody, Washington, D. C., Chairman, Council on Postgraduate Medical Education of the College, was present for all of the sessions.

Out-of-state lecturers who participated in the postgraduate course were: Dr. Chevalier L. Jackson, Philadelphia, Pennsylvania, President of the College; Andrew L. Banyai, Milwaukee, Wisconsin, Chairman, Council on International Affairs; Dr. John R. Mote, Philadelphia, Pennsylvania; Dr. Maurice S. Segal, Boston, Massachusetts, Member, Council on Postgraduate Medical Education; Dr. James M. Carlisle, Rahway, New Jersey; Dr. Jay Arthur Myers, Minneapolis, Minnesota, Editor-in-Chief, *Diseases of the Chest;* Dr. Louis L. Friedman, Birmingham, Alabama, Chairman, Committee on Occupational Diseases of the Chest; Dr. Charles P. Bailey, Philadelphia, Pennsylvania, Member, Committee on Cardiovascular Disease; Dr. Henry Welch, Washington, D. C.; and Dr. Norman J. Wilson, Boston, Massachusetts.

At a meeting of the officials of the Postgraduate Course at the Hotel New Yorker on November 13, it was agreed that the Fifth Annual Postgraduate Course will be held at the Hotel New Yorker, Nov. 10-15, 1952.

COLLEGE ESSAY AWARD

The American College of Chest Physicians offers a cash prize of two hundred fifty dollars ($250.00) for the best original contribution, preferably by a young investigator, on any phase relating to chest disease. This prize is open to contestants of all countries. Contestants are advised to study the format of *Diseases of the Chest* as to length, form and arrangement of illustrations, to guide them in the preparation of the manuscript. The following conditions must be observed:

(1) Five copies of the manuscript, typewritten in English, should be submitted to the Executive Offices, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois, not later than April 1, 1952.

(2) The only means of identification of the author or authors shall be a motto or other device on the title page, and a sealed envelope bearing the same motto on the outside, enclosing the name of the author or authors.

Committee on College Essay

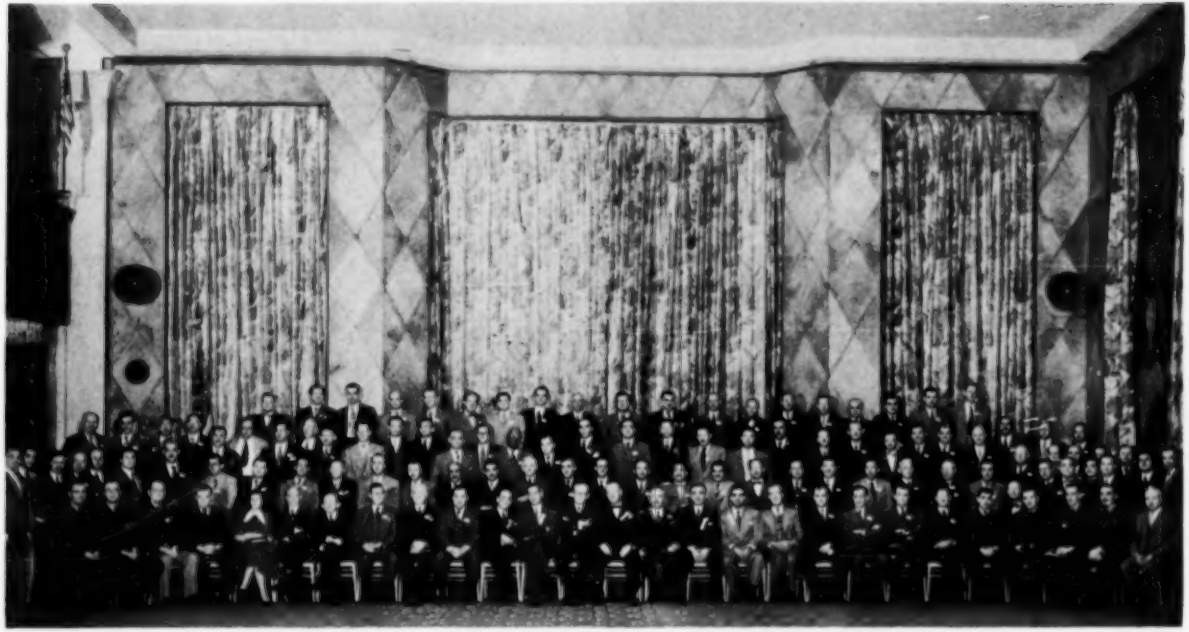
Henry C. Sweany, M.D., Chairman

E. Raymond Fenton, M.D. — Hugh L. Houston, M.D.

Joseph F. Hiatt, M.D. — David Salkin, M.D.

FOURTH ANNUAL POSTGRADUATE COURSE IN DISEASES OF THE CHEST

American College of Chest Physicians, Hotel New Yorker, New York City, November 12-17, 1951



Some of the physicians and lecturers who participated in the New York Postgraduate Course presented November 12-17, 1951.

College Chapter News

EUROPEAN CHAPTER

The first meeting of the European Chapter of the College held in Paris, France, September 15, 1951, was attended by more than 70 members and guests. Among the delegates present were: Dr. Henry Durieu, Governor of the College for Belgium; Dr. Joachim Hein, Governor for Germany; Prof. A. Omodei Zorini, Governor for Italy; Prof. Lopo de Carvalho, Regent, Portugal; Dr. Crespo Alvarez, Governor for Spain; Dr. Erik Hedvall, Governor for Sweden; Dr. Gustav Maurer, Regent, Switzerland; Dr. Robert T. Neubauer, Governor for Yugoslavia; Dr. Joseph Smart, Delegate for England; and Dr. Edgar Mayer, Chairman, Council on African and Eastern Affairs, Delegate for the United States of America.

Dr. Etienne Bernard, Regent of the College for France, introduced the following resolution: "BE IT RESOLVED, That at the joint meeting of the XII Congress of the International Union Against Tuberculosis and the II International Congress of the American College of Chest Physicians, to be held in Rio de Janeiro, Brazil, August 24-30, 1952, tuberculosis will be the principle theme of the International Union Against Tuberculosis, and non-tuberculous chest diseases will be the principle theme of the American College of Chest Physicians."

The following committee was established to discuss plans for the activities of the European Chapter and arrangements for future meetings:

Gustav Maurer, Davos, Switzerland, Chairman
Maurice Bariety, Paris, France, Vice-Chairman
Andre Meyer, Paris, France, Secretary.

The following photographs were taken at the dinner meeting of the European Chapter.

Andre Meyer, Secretary.

Delegates from left to right: Lopo de Carvalho, Lisbon, Portugal, Regent; Crespo Alvarez, Madrid, Spain, Governor; Erik Hedvall, Uppsala, Sweden, Governor; Joachim Hein, Schleswig-Holstein, Germany, Governor; Maurice Gilbert, Geneva, Switzerland; Jacques A. Delarue, Paris, France; Jean Mathey, Paris, France; Andre Meyer, Paris, France, Governor; Pierre Lefevre, Paris, France; Pierre Naveau, Amelie-les-Baines, France; Daniel Douady, Paris, France.

Delegates from left to right: Henry Joly, Haute Savore, France; Dominique Raton, Besancon, France; Pierre F. Weiller, Paris, France; Jean Marcel Lemoine, Paris, France; Julien Beerens, Gand, Belgium; Paul Veran, Nantes, France Governor; Olivier W. F. Monod, Paris, France; Jose Alix, Madrid, Spain; Edouard H. Arnold, Leysin, Vaud, Switzerland.

Delegates from left to right: Jean Mathey, Paris, France; Andre Meyer, Paris, France, Governor; Pierre Lefevre, Paris, France; Pierre Naveau, Amelie-les-Baines, France; Daniel Douady, Paris, France; Jacques Vibert, Paris, France.

Delegates from left to right: Jose Alix, Madrid, Spain; Edouard H. Arnold, Leysin, Vaud, Switzerland; Henry Durieu, Brussels, Belgium, Governor; D. Aujaleu, Director of French Ministry of Health; A. Omodei Zorini, Rome, Italy, Governor; Joseph Smart, London, England; Edgar Mayer, New York City, U.S.A., Chairman, Council on African and Eastern Affairs.

Delegates from left to right: Joseph Smart, London, England; Edgar Mayer, New York City, U.S.A., Chairman, Council on African and Eastern Affairs; Gustav Maurer, Davos, Switzerland, Regent; Etienne Bernard, Paris, France, Regent; Lopo de Carvalho, Lisbon, Portugal, Regent.

PENNSYLVANIA CHAPTER

A joint meeting of the Pennsylvania Chapter and the Laennec Society of Philadelphia was held at the Warwick Hotel, Philadelphia, November 7, and was attended by 74 physicians. Dr. Edward Lebovitz presided at the business meeting at which the following officers were elected for the coming year:

Martin J. Sokoloff, Philadelphia, President
John H. Bisbing, Reading, Vice-President
John V. Foster, Harrisburg, Secretary-Treasurer.

John V. Foster, Secretary.

NEW JERSEY CHAPTER

The fall meeting of the New Jersey Chapter was held at the Valley View Sanatorium on November 20. Dr. Edgar Mayer of New York City spoke on chronic pulmonary diseases before members of the Chapter and the Passaic County Medical Society. The next meeting of the New Jersey Chapter will be held at the Pollak Hospital for Chest Diseases, Jersey City, February 26, 1952. Dr. Samuel Cohen was appointed to arrange for speakers at the meeting.

Irving Willner, Governor for New Jersey.

WISCONSIN CHAPTER

The Milwaukee Metropolitan Section of the College met at the Medford Hotel on November 30. Dr. Leo Weinshel discussed "War Wounds of the Chest," and Dr. Donald Ausman spoke on "Flicker Photometry in Vasospastic Conditions."

Leon H. Hirsh, Secretary.

College News Notes

Dr. Laurie Lee Allen of Milwaukee addressed the Wisconsin Chapter of General Practice on "Differential Diagnosis of Diseases of the Chest," Wednesday, November 14.

Dr. Joseph S. Hiatt, Jr., of McCain, North Carolina, was re-elected Secretary-Treasurer of the Fifth District Medical Society at its Annual Fall Meeting on November 15. Dr. Hiatt was also elected counselor for the Fifth District. The counselors from each of the ten districts comprise the Executive Committee for the Medical Society of the State of North Carolina.

RESIDENT FELLOWSHIPS

The Committee on Resident Fellowships has been established for the purpose of assisting physicians in other countries who wish to take post-graduate work in the United States. For further information and resident fellowship application forms, please address the American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Committee on Resident Fellowships

Alfred A. Richman, Chairman
Emanuel Singer, Vice-Chairman
James S. Edlin, Secretary

Sydney Bassin
Harry H. Epstein
Charles E. Hamilton
Juan R. Herradora
Edward H. Robitzek
Samuel A. Thompson

ANNOUNCEMENT

Papers to be submitted for the Annual Meeting of the American Trudeau Society, May, 1952.

(1) The American Trudeau Society, Medical Section of the National Tuberculosis Association, invites the submittal of papers to be read at its next Annual Meeting in Boston, May, 1952.

(2) It is asked that a summary of the subject matter of about 200 words be sent to:

Dr. Theodore L. Badger, Chairman
Medical Sessions Committee
c/o American Trudeau Society
1790 Broadway
New York 19, New York.

not later than February 1952. It is, of course, not necessary that papers or even studies be entirely completed on this date, but in order to make up the program the Committee will need a summary on which to build.

(3) All papers will be reviewed by the Committee for the selection of the most interesting material.

(4) Papers not selected for the active program will be read "by title" and presented on the program if time permits.

(5) Subjects will include all aspects of tuberculosis, non-tuberculous respiratory and cardiac disease as well as scientific and clinical investigation with some bearing upon these subjects.

Theodore L. Badger, M.D., Chairman
Medical Sessions Committee.

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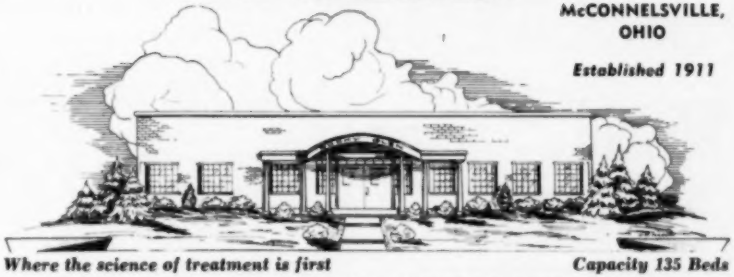

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Experienced and well trained chest specialist desirous of appointment as medical director or assistant medical director of a tuberculosis hospital. Now holding a responsible position, but contemplating change. Outstanding references. Class "A" American school graduate and native born. Please address Box 258B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

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Pres.: Dr. Segundo Huaco Vizcardo
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Secretaries: Dr. Ramon Vargas Machuca, F.C.C.P. and Dr. Jorge Campos Rey de Castro
Treas.: Dr. Carlos A. Lopez Ore
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PROGRAM FOR 1952 ANNUAL MEETING

The 18th Annual Meeting of the American College of Chest Physicians will be held at the Congress Hotel, Chicago, Illinois, June 5-8, 1952. Physicians interested in presenting their work are invited to submit titles and abstracts of their material to Dr. Harold G. Trimble, 2930 Summit St., Oakland, California, Chairman of the Committee on Scientific Program of the College.

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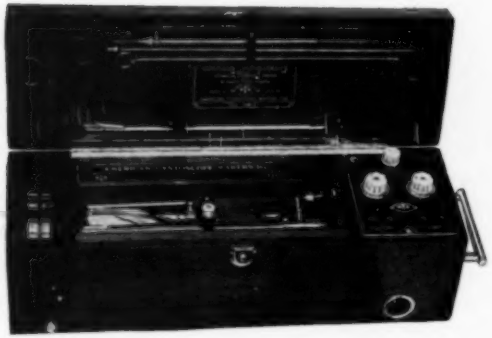

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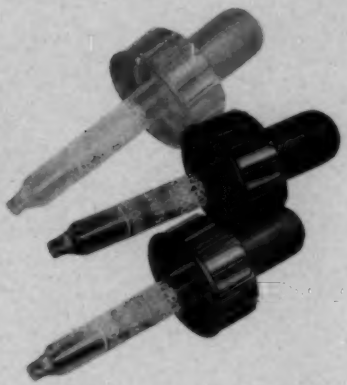

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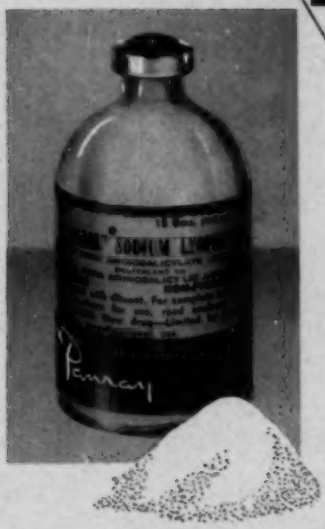

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REFERENCES: 1. "Current Status of Antimicrobial Therapy," Am. Rev. Tuberculosis, 1951, 63, 573. 2. Cutler, J. W., Extrapleural Pneumothorax in Collapse Therapy," J. Thoracic Surg., 1951, 21, 217. 3. "Meningeal and Acute Miliary Tuberculosis," Trans. 10th VA Conference Chemotherapy of Tuberculosis, January 1951, pp. 308-309.

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